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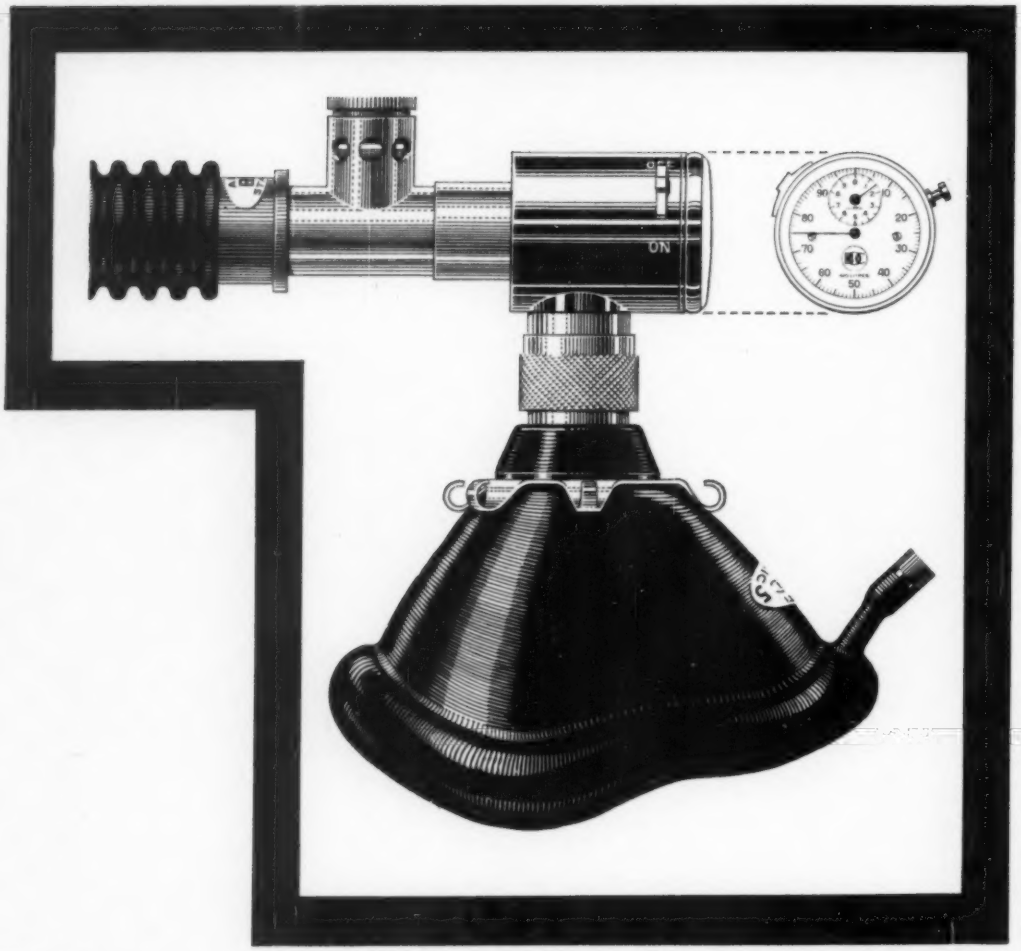

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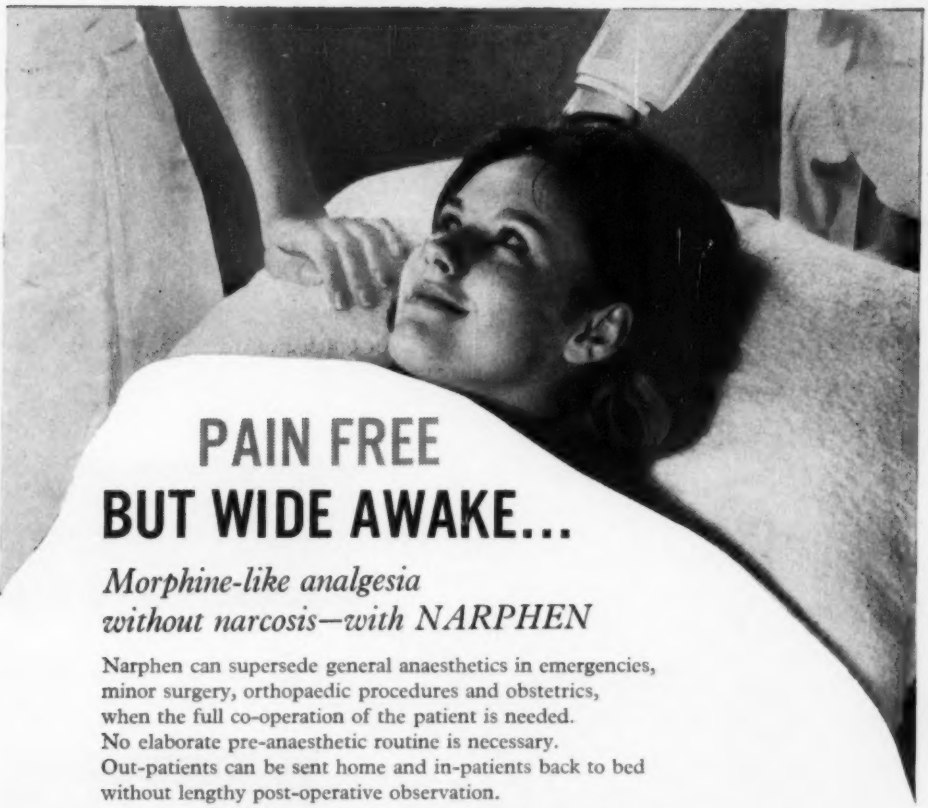

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BRITISH JOURNAL OF ANAESTHESIA

VOL. XXXIII, No. 3 MARCH 1961

EDITORIAL

DENTAL ANAESTHESIA

The credit of being the first man to administer publicly a successful general anaesthetic might well have gone to Horace Wells. A year or two before Morton's famous episode, Wells had successfully administered nitrous oxide for painless dental extraction but on attempting a public demonstration, the patient cried out when the tooth was removed, though he admitted thereafter that he had been aware of no pain. Poor Wells was labelled as a fraud with disastrous personal results. It is a solemn thought that well over one hundred years later, it is only now becoming widely recognized that there is room for considerable improvement in the conduct of dental anaesthesia.

Nitrous oxide with air or with oxygen has held pride of place these hundred-odd years for anaesthesia in the dental surgery and many are the lurid tales which have been recited of events which have accompanied its exhibition in such circumstances. The behaviour of some patients under nitrous oxide in the dental surgery has been a fruitful source of material for the humorous cartoonist and for clubroom anecdotes. The topics range from surgery to eternal rest. The squeal emitted by Wells's patient pales into insignificance and is indeed almost accepted as quite an occasional accompaniment to such an anaesthesia.

It is not to be thought, of course, that dental anaesthesia is always like this and many expert exponents have laboured mightily for advances and improvements. Under favourable conditions, and where experienced and expert dental surgeons and anaesthetists are available, the management of dental cases is exemplary—though it is noteworthy that few are agreed as to the best method of anaesthetizing such patients. The real problem lies in dealing with those patients whose dentists do not have access to trained anaesthetic help and who indeed may often have to act as surgeon and anaesthetist. Especially is this so with children; with the "difficult" patient, though the extraction may be easy; and with the difficult extractions be they few or multiple. The difficulties are not eased by the urgent need for getting the patient away speedily from the dentist's surgery. It was something of a shock to learn recently of a dental hospital which is building an extension to its premises without the provision of one bed to which a patient could be admitted during recovery from almost major oral surgery.

It is therefore heartening to learn that both the Faculty of Anaesthetists of the Royal College of Surgeons and the Association of Anaesthetists of Great Britain and Ireland have nominated committees jointly with the corresponding dental organization to study methods for improved teaching of dental anaesthesia and for advancements of a solution for the many problems associated with its widespread employment.

Further excellent news is that several centres have been organizing special courses for dental anaesthesia. This is a teaching activity which it is hoped will not only continue but spread. We would draw the attention of our readers to the symposium which is being held at the Eastman Dental Clinic in June and notice of which appears on page 172.

The increased activity in this direction is also demonstrated by the appointment of an Eli Lilly Research Fellow at the Institute of Dental Surgery (Eastman Dental Hospital) to work under the direction of Dr. Victor Goldman, and by the valuable prize which has been offered by the Association of Anaesthetists of Great Britain and Ireland for the best original essay on "Anaesthesia in the Dental Chair".

It is sincerely to be hoped that all this considerable activity will result in the rehabilitation of this Cinderella branch of anaesthesia.

Brit. J. Anaesth. (1961), 33, 126

NUMORPHAN: A NEW SUPPLEMENT TO ANAESTHESIA*

BY

MARK SWERDLOW AND P. R. BROWN
Salford Hospital Group, Manchester, England

THIS paper reports the trial of a new analgesic, Numorphan hydrochloride, as an adjuvant to thiopentone, nitrous oxide and oxygen anaesthesia.

Numorphan, 14-hydroxydihydromorphinone, is closely related chemically to morphine, as evident in figure 1.

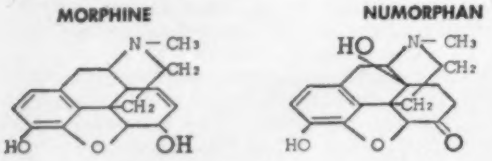

FIG. 1

In mice, Numorphan was found to have fifteen times the analgesic potency of morphine but it is only 1.5 times as toxic on subcutaneous administration (Blumberg, Carson and Stein, 1954).

METHOD

In the present work the features exhibited by Numorphan are compared with those of pethidine which was used in a similar series of cases under parallel experimental conditions (Swerdlow, Brown and Tetlow, 1960). As in the previous study of pethidine the following experimental conditions were imposed in order to demonstrate more clearly the properties of the supplementing analgesic: a single dose only of thiopentone was used and in standard dosage (7 mg/kg); no muscle relaxants were used in the maintenance of anaesthesia; the extremes of age were excluded, patients aged 18 to 60 years only being included in the series; all were in good or moderately good general condition.

Under these conditions Numorphan was employed to supplement anaesthesia in 150 patients undergoing a wide variety of operations.

CLINICAL TECHNIQUE

All patients were premedicated with morphine (8–11 mg according to size) and atropine (0.64 mg) given 1 hour before operation. Anaesthesia was induced by the intravenous injection of thiopentone sodium 7 mg/kg. If endotracheal intubation was necessary suxamethonium 30–40 mg was injected. When intubation was not required the pharynx was sprayed with local anaesthetic solution and an oral airway employed. A nitrous oxide and oxygen mixture was then administered in semi-open circuit. The initial flow rate of the gases was 2 litres of oxygen and 8 litres of nitrous oxide per minute; the flow rate of nitrous oxide was gradually reduced over a period of 10 minutes to 6 litres per minute. As soon as the administration of the gas had commenced the first dose of Numorphan was injected, either through a Gordh needle or via an intravenous drip. Numorphan does not form a clot with thiopentone so that the two agents may be administered through the same needle.

A 1-ml ampoule of Numorphan contains 1.5 mg of the drug and this was diluted to 5 ml with distilled water or normal saline. The initial dose of Numorphan was 0.3, 0.45 or 0.6 mg according to the size of the patient (i.e. 1, 1.5 or 2 ml of the solution). Thereafter supplementary doses of 0.15 to 0.3 mg of Numorphan were given when indicated by signs of lightening anaesthesia such as rapid respirations, breath holding, coughing on the tube, or grimacing, tightening of muscles or movement in response to surgical stimulation. Three to 5 minutes were allowed after an injection of analgesic for its full effect to be seen; if the patient was still insufficiently anaesthetized a

*Adapted from a paper delivered at the Annual General Meeting of the Association of Anaesthetists of Great Britain and Ireland on November 4, 1960.

further dose of analgesic was given. Whenever the breathing was depressed during anaesthesia the respirations were assisted. At the end of anaesthesia levallorphan tartrate 0.5 to 1 mg was administered if the respiratory exchange was considered inadequate. Finally the time taken for the return to consciousness and the presence or absence of coughing on the tube at that time were noted.

RESULTS

Table I shows the sex and average age and weight distribution of the present patients, together with those of the (previous) pethidine series. Statistical analysis* shows that the two populations are homogenous.

TABLE I
Distribution of cases.

	Pethidine		Numorphan	
	Male	Female	Male	Female
% of patients	37	63	46	54
Average age (years)	42	44	42	41
Average weight (kg)	70	62	71	60

TABLE II
Operations performed.

Operation	Number of cases	
	Numorphan	Pethidine
Varicose veins	51	40
Colporrhaphy	5	16
E.N.T.	19	9
Orthopaedic	18	18
Breast operations	7	11
Genital	16	8
Hernia	24	11
Miscellaneous	10	7
Total	150	120

Table II shows the operations performed in the two drug series. The duration of anaesthesia in the two series is analyzed in table III. Statistical analysis shows no significant difference in the duration of the operations in the two series ($\chi^2 = 11.56$). Table IV shows the average dose of each analgesic agent required to achieve a settled

* For purposes of evaluation all the data in this study were arranged in an appropriate number of classes ranging from minimal to maximal values and submitted to tests of significance between the pethidine and Numorphan series. The conventional level of significance is expressed as P = or <0.05. The values of P are given but in the interests of brevity the mean values (arithmetic or geometric according to suitability) are used to summarize the individual frequency distributions on which the tests were conducted.

TABLE III
Duration of anaesthesia.

Duration of anaesthesia (minutes)	Percentages of cases	
	Numorphan	Pethidine
0–30	20	17
31–60	49	44
61–90	20	30
91–120	10	7
121–150	1	2

state of anaesthesia (that is the amount given in the first 15 minutes of anaesthesia) and the average total doses for each drug series. By averaging the respective figures in table IV it will be seen that the relative potency of Numorphan and pethidine is about 60:1. The settling dose of pethidine represented 69 per cent of the total dose, while that of Numorphan represented 89 per cent of the total dose. The average duration of effect of the 0.3, 0.45 and 0.6 mg doses of Numorphan was 22, 26.4 and 26.8 minutes respectively. In comparison, 20 mg of pethidine was found to have a duration of action of 16 minutes.

Maintenance of anaesthesia.

Using either agent, once the patient has settled under a nitrous oxide and oxygen mixture the maintenance of anaesthesia demands solely the periodic injection of supplementary doses of analgesic in response to signs of lightening anaesthesia. Maintenance of a smooth, level anaesthesia was found to be easier with Numorphan than with pethidine. This is partly because of the greater potency of Numorphan and partly because of the longer duration of its action. However, with both adjuvants, despite the allowance of adequate time for settling and take-up of nitrous oxide, this anaesthetic technique is occasionally unsatisfactory, especially in stocky, muscular individuals and in heavy smokers and alcoholics. The deficiencies are shown by recurring movement, repeated breath holding and spasm on the endotracheal tube and recurring bursts of coughing. In addition it is sometimes necessary to administer a further dose of 50 to 100 mg of thiopentone to settle the patients. The incidence of these undesirable features is analyzed in table V, which also shows that the Numorphan series of patients tolerated an endotracheal tube better than those who received pethidine supplementation. It may be added that in some cases the

TABLE IV
Dosage.

Drug series	Average dose to settle (mg)	Average total dose (mg)	Average dose (mg/min)	Average dose (mg/kg)
Numorphan	0.63	0.89	0.02	0.013
Pethidine	38.4	55.5	1.2	0.79

patients were turned from the face-down to the supine position during the course of varicose vein surgery. In the pethidine group eleven patients were thus turned and all required a further dose of pethidine before they would settle; in the Numorphan group, of the eleven patients who were turned over only two required a further dose of Numorphan to settle them. Fewer patients showed repeated movement in the Numorphan group; moreover, when movement did occur in response to stimulation it was much less marked and less forcible than when pethidine was the adjuvant employed.

On the other hand the incidence of respiratory depression was greater in the Numorphan series. In both series some patients exhibited more than one of these undesirable features. During anaesthesia the pupils were almost invariably markedly contracted. Wealing along the course of the injected vein was not seen with Numorphan.

TABLE V
Inadequacies during anaesthesia.

Feature	Percentage of patients in Numorphan series	Percentage of patients in pethidine series
Repeated movement	6	11
Breath holding	7	7
Coughing	7	13
Respiratory depression	11	8
Required extra thiopentone	7	5

Respiration.

Table V shows that an undue degree of respiratory depression occurred in 8 per cent of patients of the pethidine series and in 11 per cent of patients in the Numorphan series. This was usually due to relative overdosage and it most commonly followed the initial dose. The average respiration rate of the patients in the Numorphan series was 13 per minute and of those in the pethidine series was 13.5 per minute. The mean minimal respiration rate in the Numorphan series was 8.9 and in the pethidine series was 10.3. Analysis shows that the average respiration rates in the two series were not significantly different ($\chi^2 = 15.83$; $P = 0.04$) but the mean of the minimal respiration rates was significantly lower in the Numorphan series ($\chi^2 = 16.833$; $P = 0.02$).

Circulatory changes.

There were no consistent differences in the blood pressure and pulse records of the patients of the two drug series.

Recovery.

Recovery of consciousness was generally rapid. The mean time between discontinuing the nitrous oxide and oxygen mixture and awakening (as judged by the patient's ability to obey commands or open the eyes in response to light tactile stimulation) was 4.1 minutes with pethidine and 2.8 minutes with Numorphan. There is a significant difference between these recovery times ($P < 0.001$; $\chi^2 = 32.7$). The quicker awakening after Numorphan suggests that it has a less marked sedative action, an attribute which has also been reported by Coblentz and Bierman (1956) and by Samuels et al. (1959).

The rapid recovery of consciousness was accompanied by early return of the cough reflex; 61 per cent of the Numorphan patients and 62 per cent of the pethidine patients coughed on the endotracheal tube within 3 minutes after stopping administration of the nitrous oxide and oxygen mixture. Table VI shows the cough record in those cases where this feature was recorded (in patients who had been intubated).

TABLE VI

Feature	% of recorded cases	
	Numorphan	Pethidine
Coughed before awakening	56	60
Coughed after awakening	9	7
Coughed and awoke simultaneously	12	14
Did not cough	23	19

Nausea and/or vomiting* occurred in 45 per cent of the patients in the Numorphan series (of 119 cases recorded) and in 64 per cent of the pethidine series (of 73 cases recorded). No useful evaluation of postoperative pain was found possible during the study but an investigation of the value of Numorphan for postoperative pain relief is now in progress.

Relative potency.

Coblentz and Bierman (1956), in studies of the relief of postoperative pain found a potency ratio of 50:1 for Numorphan and pethidine. Wallenstein and Houde (1956) in "double blind" studies of pain due to cancer found that morphine 10 mg had a similar analgesic potency to Numorphan 1.12 mg. Assuming the equivalence accorded by Nathan (1952) to morphine and pethidine (morphine 16 mg $\equiv$ pethidine 125 mg), pethidine 100 mg would, according to Wallenstein and Houde, approximate in potency to Numorphan 1.34 mg. In the present work Numorphan has been found to be about sixty times as potent as pethidine, a ratio which is in agreement with those of the previous workers.

CONCLUSIONS

No other report of the use of Numorphan as an adjuvant to anaesthesia has yet appeared. In the present study in operations not requiring the employment of muscle relaxants the use of Numorphan has enabled smooth anaesthesia to be achieved in a higher percentage of patients than when anaesthesia was supplemented with pethidine. The use of Numorphan has also led to a reduced incidence of coughing on the tube during anaesthesia and to earlier postoperative recovery of consciousness.

The authors consider that Numorphan merits more extensive trial as an adjuvant to anaesthesia.

*Nausea and vomiting signifies "any nausea, retching or vomiting occurring after the end of the operation, whether remembered or not", as defined by Riding (1960).

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FURTHER EXPERIENCES WITH METHYLATED THIOBARBITURATES

BY

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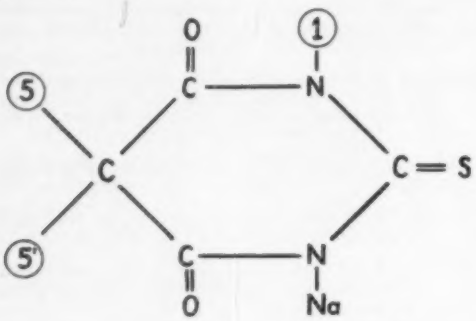
IN a recent publication, Dundee, Barron and King (1960) reported that methylation of the thiobarbiturate, Inactin, produced a compound (B.137) which caused a prohibitively high incidence of spontaneous abnormal muscle movements. It was concluded that the drug was unsuitable for clinical use.



Drug	1	5	5'
Thiopentone	H	$CH_3 \cdot CH_2$	$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH(CH_3)$
Buthalitone	H	$CH_2 \cdot CH = CH_2$	$CH(CH_3) \cdot CH(CH_3) \cdot CH_3$
B.82	CH_3	$CH_2 \cdot CH = CH_2$	$CH(CH_3) \cdot CH(CH_3) \cdot CH_3$
B.133	CH_3	$CH_2 \cdot CH_2$	$CH(CH_3) \cdot CH(CH_3) \cdot CH_3$

FIG. 1
Formulae of the drug under study.

Limited supplies of two further methylated thiobarbiturates, described by Peel et al. (1959), known as B.82 and B.133 have become available. The formulae of these are shown in figure 1 and it can be seen that B.82 is the methylated form of buthalitone. B.133 is not related chemically to any thiobarbiturate in clinical use, being sodium N-methyl 5-ethyl 5'-isobutyl thiobarbiturate. This paper reports on a clinical trial of these two compounds in which their effects are compared with those of thiopentone and buthalitone.

METHOD OF STUDY

This was identical to that described by Dundee and Moore (1961), the anaesthesia used being limited to thiobarbiturate, nitrous oxide and oxygen, and all the operations were for cervical dilatation and uterine curettage. Atropine 0.6 mg was the standard premedication throughout the study. Observations were made on the incidence of various complications following the induction of anaesthesia and each administration was graded according to the classification of Dundee and Riding (1960).

RESULTS

It can be seen from table I that the series of cases with each drug is comparable as regards age and weight.

There can be no doubt from the results that methylation of buthalitone (B.82) produces a compound which not only possesses the disadvantages of the parent drug with regard to respiratory disturbances but, in addition, causes a dramatically high increase in the incidence rate of excitatory phenomena. Slightly more than half the patients developed a generalized erythematous rash within one minute of injection of B.82, a complication which was not seen with either buthalitone or thiopentone.

TABLE I

Details of patients and percentage incidence of induction complications with the four compounds under study.

Drug	Thiopentone	Buthalitone	B.82	B.133
No. of cases	100	50	25	13
Average age	31.20 ± 1.29	31.54 ± 1.06	29.64 ± 1.52	32.00 ± 2.03
Average weight (kg)	59.64 ± 1.69	59.84 ± 1.44	59.12 ± 1.38	62.85 ± 4.32
Induction dose (mg/kg)	3.83 ± 0.05	10.14 ± 0.42	10.15 ± 0.60	6.63 ± 0.12
Total dose (mg/kg)	4.87 ± 1.27	12.25 ± 0.74	10.69 ± 0.54	9.68 ± 0.52
Excitatory phenomena				
Tremors	3	10	80	46
Muscle movements	2	26	96	54
Nil	95	66	0	31
Respiratory upset				
Cough and/or hiccough	6	48	88	46
Laryngospasm	1	4	8	0
Nil	94	44	12	54
Marked respiratory depression	2	2	8	0
Severe hypotension	3	18	16	8
Venous thrombosis	6	0	0	23
Nausea and/or vomiting	17	4	16	15
Erythematous rash	0	0	52	31
Induction grades				
1	81	22	0	15
2	18	72	8	39
3	1	6	92	46

Following B.133 the frequency of side effects were not so great and the severity of these side effects not so marked as after B.82, but the incidence of excitatory phenomena was still significantly higher than with the nonmethylated thiobarbiturates. The incidence of respiratory side effects was similar to that for buthalitone. The frequent occurrence of a generalized erythematous rash was also a feature of B.133. In comparison with the other three compounds under study, the latter drug caused a high incidence of postoperative venous thrombosis.

It is interesting to note the similarity of the average induction doses of buthalitone and B.82, suggesting that methylation does not affect the potency of the thiobarbiturates. This confirms previous observations reported by Dundee, Barron and King (1960).

DISCUSSION

Since grade 3 anaesthesia (classification of Dundee and Riding, 1960) indicates that the administration was either totally unsatisfactory from the surgeon's point of view or dangerous to the patient, it can be seen that the methylated thiobarbiturates are unsatisfactory for clinical use. From our experience with these compounds, together with that of Stoelting (1953), it would seem that the methylated thiobarbiturates are unlikely to have any place in anaesthetic practice.

ACKNOWLEDGMENTS

Our thanks are due to Drs. L. Banks, and F. A. Robinson, of Allen and Hanbury Ltd., for supplies of B.82 and B.133, and to Dr. J. Harper, of May and Baker Ltd., for thiopentone and buthalitone. We are indebted to Mr. H. I. McClure and the staff of the gynaecological department of Musgrave Park Hospital for providing facilities for this investigation.

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THE CONTROL OF BRAIN VOLUME AND TENSION DURING INTRACRANIAL OPERATIONS

BY

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THE control of brain volume during intracranial operations is one of the major problems in neurosurgery and one of the most difficult to solve. Some of the hypothetical aspects of physiopathology in this field are as yet rather obscure and the various solutions which have been put forward are not easy to evaluate. It is difficult to gauge their efficacy because a simple and practical method for the measurement of the tension of the dura mater and the brain during intracranial operations does not exist.

In this paper the methods and techniques which have been adopted during the last two years, in the Neurosurgical Clinic of Milan University, will be discussed. These have proved to be the most suitable for obtaining the state of cerebral hypotension that is such an essential feature of a good operating field in neurosurgery.

MATERIAL AND METHODS

The data were collected during the course of 330 intracranial operations performed under general anaesthesia.

In each case the following factors were taken into consideration.

In the pre-operative stage.

The existence of intracranial space-occupying lesion, of inflammatory processes or subarachnoid haemorrhage and the presence and seriousness of clinical or radiological signs of raised intracranial tension, especially of disturbances of consciousness were noted and according to the findings the patients were divided into five classes, as follows:

Class I. Patients without space-occupying lesions and without raised intracranial tension. Examples of these are trigeminal neuralgia, epilepsy, pituitary adenomata without suprasellar expansion, intracranial aneurysms not associated with recent haemorrhage, dyskinetic syndrome.

Class II. Patients with space-occupying lesions but without clinical or radiological signs of raised intracranial tension. These included solid or cystic neoplasms, haematomata.

Class III. Patients with clinical and/or radiological signs of slightly or moderately raised intracranial tension (as in class II and including also abscesses and internal hydrocephalus).

Class IV. Patients with clinical and radiological signs of markedly raised intracranial tension, but without disturbances of consciousness (pathological findings as in class III).

Class V. Patients with a decompensated rise in intracranial tension and with disturbance of consciousness (as in classes III and IV, and including ruptured aneurysms with recent subarachnoid haemorrhage).

In certain calculations classes II and III, as well as classes IV and V, were considered together.

During operation.

The type of anaesthesia, the respiratory rate and minute volume and the position of the patient on the operating table were recorded.

In order to estimate the tension of the dura mater and of the underlying brain very simple criteria based on visual observation and palpation were adopted as it was not possible, for obvious practical reasons, to resort to more accurate means of gauging this tension such as those suggested by Lundberg, Kjallquist and Bien (1959).

The dura mater was defined as hypotensive if, upon the theca being opened, it appeared wrinkled and depressed in relation to the bone edges (for quantitative evaluation this was classified in arbitrary units as degree 1); normotensive when it was slightly convex but pulsating and easily depressible (degree 2); slightly tense or tense when, whilst more or less resistant to palpation, it could be opened without injury to the underlying cerebral tissue (degree 3 and degree 4 respectively); hypertensive when special measures were necessary at the time of opening to prevent laceration and herniation of the nervous tissue (degree 5). These

arbitrary units were used for the calculation of averages in order to allow a statistical comparison of data.

As means of controlling the tension, the following procedures were examined: (*a*) drainage of cerebrospinal fluid either by ventricular or lumbar puncture; (*b*) osmotic dehydration by the administration of hypertonic solutions (30 per cent urea or 50 per cent sucrose in doses of 3 to 5 ml/kg bodyweight, by intravenous drip); (*c*) induction of controlled hypotension by means of adrenolytic or ganglion blocking drugs; (*d*) the use of drugs which exert a constrictive action on cerebral vessels or respiratory stimulants; (*e*) the induction of moderate hypothermia; and (*f*) the use of controlled hyperventilation (min vol 10 to 15 l.), effected either manually, by intermittent positive pressure, or mechanically by means of a positive-negative (subatmospheric) respiration pump (Engström respirator).

A record was made of whether these measures had been used prophylactically or at the time when the dura was exposed or already opened.

RESULTS

In attempting to analyze the results it was realized that, in order to estimate the efficacy of the control measures adopted in each case, it was first essential to determine the extent to which the variable pre-operative and intra-operative factors affected the tension of the dura mater.

Analysis of the variable factors.

For this preliminary evaluation, only the untreated cases were considered.

Raised intracranial tension syndrome.

The great majority of patients (70 per cent) were affected with space-occupying lesions or with internal hydrocephalus. In most of these patients there were clinical symptoms and signs of more or less serious elevations of intracranial tension.

In figures 1A and 1B the case records are classified into five groups according to the presence and seriousness of raised intracranial tension following the criteria already described. The distribution of case records in these five classes according to the different degrees of dural tension strongly suggested that there was a proportional relationship between the degree of elevation of the intracranial tension and the occurrence and gravity of the abnormal tension of the dura mater on opening the theca. In fact, by plotting, for each case, the level of the pre-operative condition against the degree of observed dural tension, both measured in arbitrary units from 1 to 5, a significant correlation was found ($r = 0.52$, with $P < 0.001$) between the two data (table IA, concerning untreated cases).

General anaesthesia.

General anaesthesia was induced in every patient using a small dose of thiopentone (200 to 300 mg). Endotracheal intubation was performed, after a full dose of suxamethonium and topical anaesthesia with lignocaine, using an armoured latex tube of the widest permissible bore. Only in a few patients was halothane substituted for thiopentone (for example epileptics undergoing corticography). Anaesthesia was maintained using nitrous oxide and oxygen and ether, halothane, trichloroethylene or pethidine in a non-rebreathing system with minimal resistance.

Figure 1A shows that an abnormal tension of the dura mater was only rarely found in the group of patients without tumours or raised intracranial tension. It would seem, therefore, justifiable to conclude that general anaesthesia did not appreciably modify the conditions of the operating field.

An attempt was made to examine the undesirable effect of ether. Untreated patients without space-occupying lesions (class I) were considered. These were divided according to two principal types of anaesthesia. Anaesthesia in the first group was maintained using nitrous oxide with oxygen and ether. In the second group pethidine and sometimes potentiating drugs, or trichloroethylene supplemented nitrous oxide and oxygen. All these patients were breathing spontaneously. From figure 2 and table II it is clear that the use of ether, at least up to a concentration of 3 to 4 volumes per cent, had no injurious effect on the tension of the dura mater.

The number of patients in which other types of anaesthesia were used was not sufficient to enable the many factors involved to be considered (existence or not of raised intracranial tension, type of therapy, etc.) and therefore a valid comparison between the procedures could not be made.

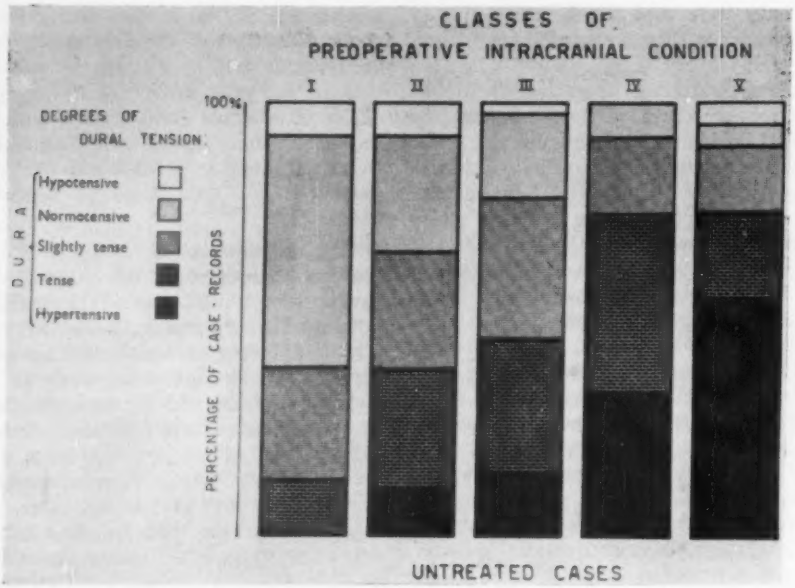

FIG. 1A

Relationship between pre-operative intracranial condition and dural tension found in untreated patients at craniotomy.

Class I: patients without space-occupying lesions and without intracranial hypertension.
Class II: patients with space-occupying lesions but without intracranial hypertension.
Class III: patients with slightly or moderately raised intracranial tension.
Class IV: patients with severely raised intracranial tension.
Class V: patients in coma due to very high intracranial tension or subarachnoid haemorrhage.

TABLE IA

Relationship between pre-operative intracranial condition and dural tension in untreated patients at craniotomy.

Dural tension	Classes of pre-operative intracranial condition					Total
	I	II	III	IV	V	
Degree 1: Hypotensive	4	2	1	0	1	8
Degree 2: Normotensive	29	7	8	1	1	46
Degree 3: Slightly tense	14	7	13	2	3	39
Degree 4: Tense	7	7	13	5	4	36
Degree 5: Hypertensive	0	3	6	4	11	24
Total of cases	54	26	41	12	20	153

Absolute numbers for figure 1A. $r = 0.52$; $P < 0.001$.
Correlation between classes of pre-operative intracranial condition and degrees of dural tension was calculated from arbitrary units.

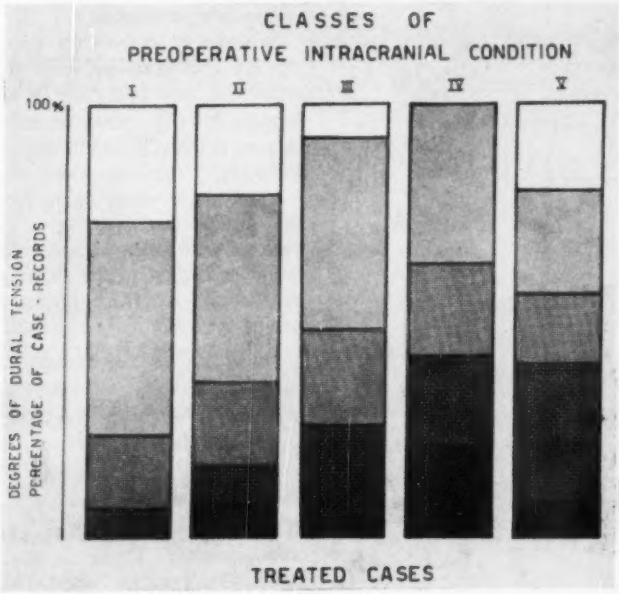

FIG. 1B

Relationship between pre-operative intracranial condition and dural tension found at craniotomy; only treated patients are considered.

For explanation of histogram see figure 1A.

TABLE IB

Relationship between pre-operative intracranial condition and dural tension in treated patients at craniotomy.

Dural tension	Classes of pre-operative intracranial condition					Total
	I	II	III	IV	V	
Degree 1: Hypotensive	12	8	4	0	5	29
Degree 2: Normotensive	22	17	24	5	6	74
Degree 3: Slightly tense	8	7	12	3	4	34
Degree 4: Tense	3	4	12	3	8	30
Degree 5: Hypertensive	0	3	2	3	2	10
Total of cases	45	39	54	14	25	177

Absolute numbers for figure 1B.

$r = 0.28$; $P < 0.001$.

Correlation between classes of pre-operative intracranial condition and degrees of dural tension was calculated from arbitrary units.

The difference between r_A and r_B is significant (as difference between Z_A and Z_B: $t=2.58$; $P=0.01$).

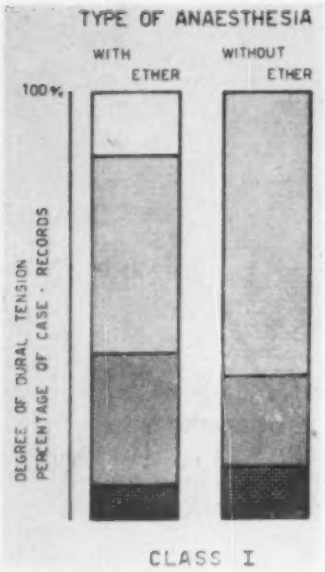

FIG. 2

Influence of ether anaesthesia on dural tension at craniotomy.

For explanation of histogram see figure 1A.

Only Class I (without space-occupying lesion) is considered, as the number of untreated patients "without ether" in the other classes was too low.

TABLE II

Influence of ether anaesthesia on dural tension.

Dural tension	Maintenance of anaesthesia	
	with ether	without ether
Degree 1	4	0
Degree 2	12	16
Degree 3	8	5
Degree 4	2	3
Degree 5	0	0
Total of cases	26	24
Mean degree of dural tension	2.31	2.46

Absolute numbers for figure 2. Only untreated patients of Class I are considered. The difference between averages of dural tension is insignificant ($t = 0.019$; $P > 0.9$).

Pulmonary ventilation.

In order to analyze the possible effect of pulmonary ventilation on dural tension the alveolar ventilation rate was roughly calculated from the formula $\dot{V}E - (f \times 100)$, where $\dot{V}E$ is the expired minute volume in millilitres, measured by a dry gasmeter, f the respiratory rate per minute and 100 ml an arbitrary value for the deadspace of the intubated air passages, in the adult. The patients were grouped under three levels of ventilation according to the mean values of "alveolar ventilation" recorded during the half-hour preceding the opening of the skull as follows:

hypoventilation—alveolar ventilation of 3,000 ml or less;

normal range—alveolar ventilation between 3,000 and 7,000 ml;

hyperventilation—alveolar ventilation greater than 8,000 ml.

The patients in the first two groups respired spontaneously. Those in the third group were artificially hyperventilated, either manually with the Ambu-Ruben system or, more often, with intermittent positive-negative pressure by means of the Engström respirator. It was ascertained that there was no apparent correlation between the levels of ventilation during operation and the pre-operative intracranial condition; that is to say, the different rates of ventilation were distributed at random in each group of intracranial tension (χ^2 between "hypo-", "normo-", or "hyperventilation" and groups I, II, and III, and IV and V = 3.095 with $P > 0.5$).

All untreated patients could therefore be grouped into a single class, disregarding the differences in the pre-operative intracranial condition.

The graphs in figure 3 suggest a close relationship between the level of ventilation and the degree of dural tension. Nevertheless, the averages of dural tension calculated for the different levels of ventilation (table III), although higher for hypoventilating patients and much lower for hyperventilated patients, did not differ significantly when analyzed both in couples with Student's t-test, or globally with the analysis of variance (f in every case being between 10 and 20 per cent).

A significant difference between ventilations

TABLE III

Influence of pulmonary ventilation on dural tension.

	Classes of pre-operative intracranial condition								
	I			II + III			IV + V		
Dural tension	hypo-	normo-ventilation	hyper-	hypo-	normo-ventilation	hyper-	hypo-	normo-ventilation	hyper-
Degree 1	1	2	0	0	3	0	0	1	0
Degree 2	5	18	7	1	12	6	0	2	1
Degree 3	5	7	2	4	15	0	1	3	0
Degree 4	2	2	0	5	13	2	1	7	2
Degree 5	0	0	0	1	4	1	5	10	0
Total of cases	13	29	9	11	47	9	7	23	3
Mean degree of dural tension	2.62	2.31	2.22	3.54	3.06	2.78	4.57	4.00	3.33

Absolute numbers for figure 3. Only untreated cases are considered.
All differences between averages of dural tension are below the level of statistical significance (P between 0.1 and 0.2).
χ^2 test—all classes grouped together for distribution between "not tense" (degrees 1 and 2) and "tense duras" (degrees 3, 4 and 5)—gives:

for the three levels of ventilation $\chi^2 = 10.25$; $P < 0.01$
for hypo- and normoventilation $\chi^2 = 1.95$; P between $0.20 > P > 0.10$
for hypo- and hyperventilation $\chi^2 = 8.35$; $P < 0.01$
for normo- and hyperventilation $\chi^2 = 4.54$; P between $0.05 > P > 0.02$

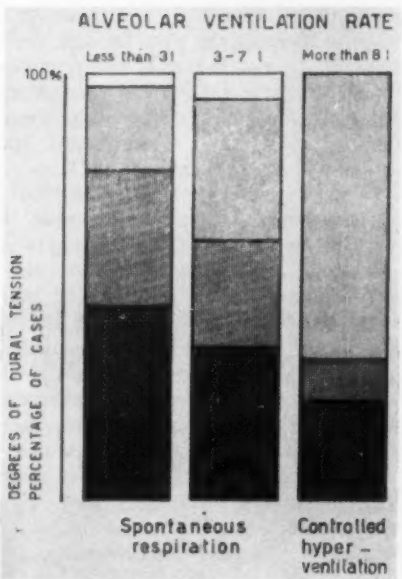

FIG. 3

Influence of pulmonary ventilation on dural tension. For explanation of histogram see figure 1A. Untreated cases of all classes of pre-operative condition are considered together.

was found, on the contrary, if the case records were grouped under only two headings of dural tension (hypo- or normotensive, and more or less tense) and analyzed with the χ^2 test. The biggest difference was observed between the hypoventilating and the hyperventilated patients; a lower, but still significant difference could be ascertained for patients with a "normal" ventilation compared with hyperventilated ones; while even with this simplified test the difference between the hypo- and the normoventilating patients was below the level of statistical significance.

Position on the operating table.

The untreated patients were divided into three groups according to whether they had been operated in a lying position with the operating table moderately inclined, head up; in a prone position; or in a sitting or sharply tilted position. The following observations were made. Disregarding the different intracranial pre-operative states (fig. 4), the percentages of patients with tense or hypertensive duras then appeared almost equal for the first two positions and much lower for the sitting position. However, no significant difference between the means of dural tension could be demonstrated (table IV).

TABLE IV

Influence of posture on dural tension.

	Classes of pre-operative intracranial condition					
	I			II + III		
Dural tension	Supine	Prone	Sitting	Supine	Prone	Sitting
Degree 1	2	0	2	1	0	2
Degree 2	21	3	5	12	3	0
Degree 3	7	2	5	17	3	0
Degree 4	3	3	1	18	2	0
Degree 5	0	0	0	9	0	0
Total of cases	33	8	13	57	8	2
Mean degree of dural tension	2.33	3.00	2.38	3.39	2.88	1.00

Absolute numbers for figure 4, but divided into two classes of pre-operative condition. The difference between averages for prone and sitting patients in Class I is not significant: ($t = 1.59$; P between $P\ 0.20 > P > 0.10$). Only untreated patients are considered.

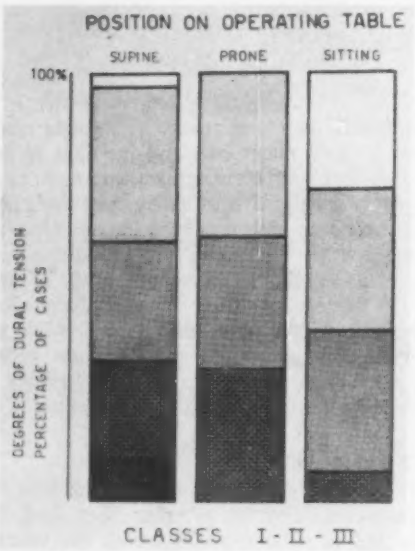

FIG. 4

Influence of posture on dural tension.
For explanation of histogram see figure 1A.
All patients are untreated. Only Classes I, II and III of pre-operative intracranial condition are considered, as sitting-up or prone patients are not present in Classes IV and V.

Analysis of the methods of control.

In the evaluation of treatments, it was deemed necessary to take into account the pre-operative intracranial condition of the patients, while no special selection was made for other factors, such as the type of anaesthesia, the variations of spontaneous respiration and the position on the operating table, which had been shown to have a negligible effect on the dural tension. Artificial hyperventilation was included among the means of control of brain volume and tension tested, as well as cerebrospinal fluid drainage from the ventricles or spinal subarachnoid spaces, osmotic dehydration by means of 50 per cent sucrose, or 30 per cent urea, the induction of controlled hypotension and hypothermia. Each method was used either prophylactically or when the dura mater was already exposed (with the single exception of hypothermia, which was always induced before the opening of the theca) and its efficacy was tested both when used alone or in combination with one or more of the others. For the sake of simplicity, all instances of multiple methods were grouped together. A preliminary analysis of data demonstrated that adrenolytic drugs, such as hydergine, chlorpromazine, respiratory stimulants and cerebral vasoconstrictors, such as aminophylline, were ineffective in lowering dural tension. These agents were therefore excluded from the group of therapeutic methods. The effect of the treatments, considered together, is clearly shown in figure 1B in comparison with figure 1A. In every class of pre-operative condition the percentages

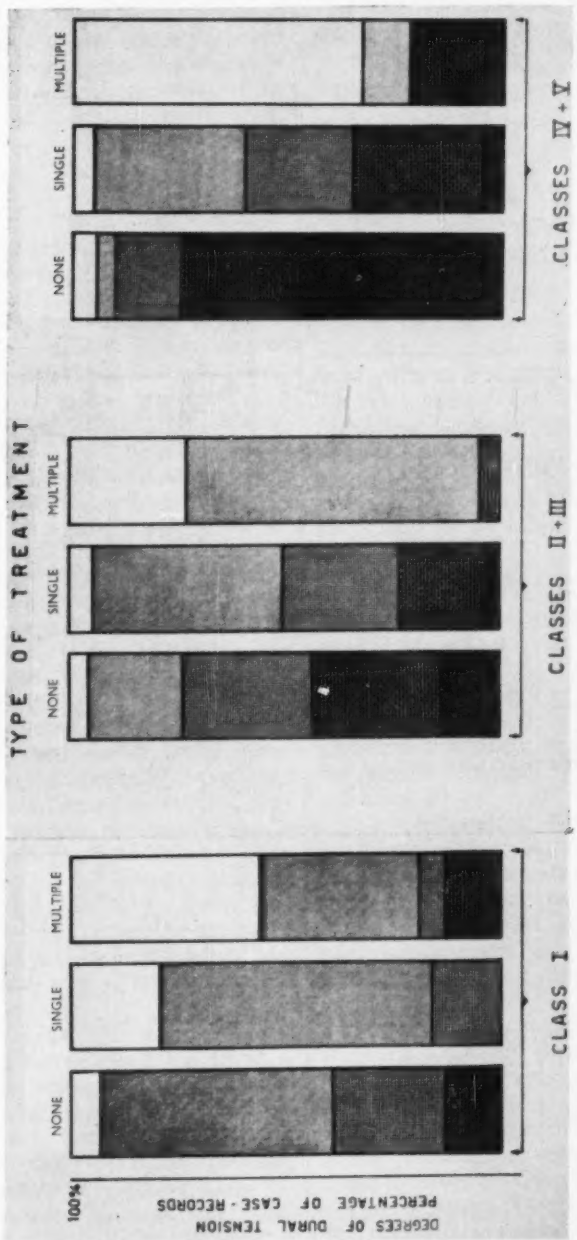

FIG. 5

Effect of single and multiple treatments on dural tension.
For explanation of histogram see figure 1A.
The treatments were applied before exposure of the dura. Single treatments, here grouped together, are: CSF drainage, controlled hypotension, osmotic dehydration, artificial hyperventilation.

TABLE IV

Influence of posture on dural tension.

	Classes of pre-operative intracranial condition					
	I			II + III		
Dural tension	Supine	Prone	Sitting	Supine	Prone	Sitting
Degree 1	2	0	2	1	0	2
Degree 2	21	3	5	12	3	0
Degree 3	7	2	5	17	3	0
Degree 4	3	3	1	18	2	0
Degree 5	0	0	0	9	0	0
Total of cases	33	8	13	57	8	2
Mean degree of dural tension	2.33	3.00	2.38	3.39	2.88	1.00

Absolute numbers for figure 4, but divided into two classes of pre-operative condition. The difference between averages for prone and sitting patients in Class I is not significant: ($t = 1.59$; P between P 0.20 > P > 0.10). Only untreated patients are considered.

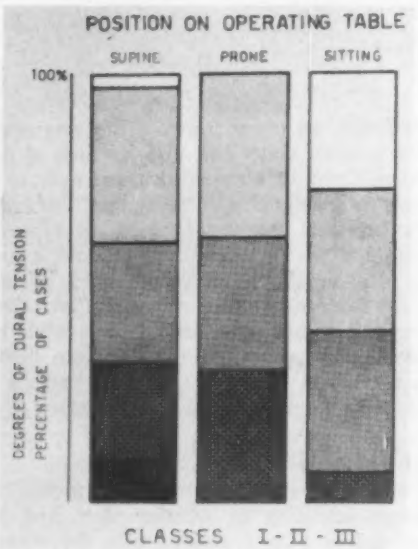

FIG. 4

Influence of posture on dural tension.
For explanation of histogram see figure 1A.
All patients are untreated. Only Classes I, II and III of pre-operative intracranial condition are considered, as sitting-up or prone patients are not present in Classes IV and V.

Analysis of the methods of control.

In the evaluation of treatments, it was deemed necessary to take into account the pre-operative intracranial condition of the patients, while no special selection was made for other factors, such as the type of anaesthesia, the variations of spontaneous respiration and the position on the operating table, which had been shown to have a negligible effect on the dural tension. Artificial hyperventilation was included among the means of control of brain volume and tension tested, as well as cerebrospinal fluid drainage from the ventricles or spinal subarachnoid spaces, osmotic dehydration by means of 50 per cent sucrose, or 30 per cent urea, the induction of controlled hypotension and hypothermia. Each method was used either prophylactically or when the dura mater was already exposed (with the single exception of hypothermia, which was always induced before the opening of the theca) and its efficacy was tested both when used alone or in combination with one or more of the others. For the sake of simplicity, all instances of multiple methods were grouped together. A preliminary analysis of data demonstrated that adrenolytic drugs, such as hydergine, chlorpromazine, respiratory stimulants and cerebral vasoconstrictors, such as aminophylline, were ineffective in lowering dural tension. These agents were therefore excluded from the group of therapeutic methods. The effect of the treatments, considered together, is clearly shown in figure 1B in comparison with figure 1A. In every class of pre-operative condition the percentages

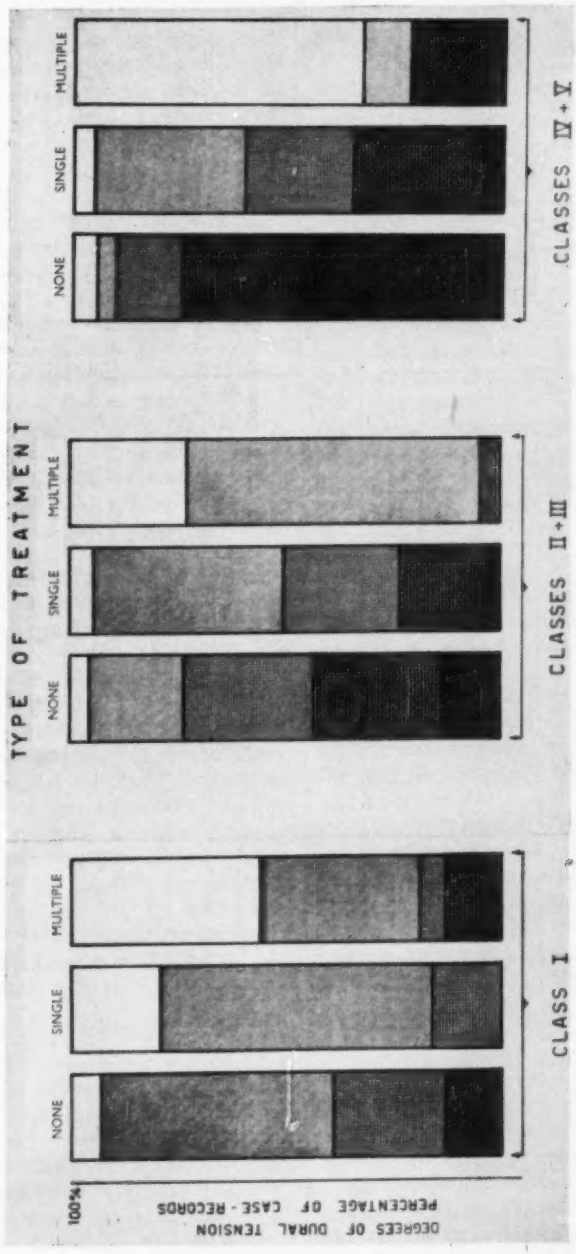

FIG. 5

Effect of single and multiple treatments on dural tension.
For explanation of histogram see figure 1A.
The treatments were applied before exposure of the dura. Single treatments, here grouped together, are: CSF drainage, controlled hypotension, osmotic dehydration, artificial hyperventilation.

TABLE V

Effect of single and associated treatments on dural tension

	Classes of pre-operative intracranial condition																						
	I							II + III							IV + V								
Dural tension	No tr.	CSF dr.	Osm.	Hypots.	I.P.P.R.	Hypothr.	M.M.	No tr.	CSF dr.	Osm.	Hypots.	I.P.P.R.	Hypothr.	M.M.	No tr.	CSF dr.	Osm.	Hypots.	I.P.P.R.	Hypothr.	M.M.		
Degree 1	4	1	1	2	0	2	7	3	0	2	1	0	1	6	1	1	0	0	0	0	6		
Degree 2	29	2	3	0	7	3	6	15	10	7	1	6	4	15	2	3	2	1	1	1	1		
Degree 3	14	0	1	0	2	4	1	20	4	9	2	0	4	0	5	1	2	2	0	2	0		
Degree 4	7	0	0	0	0	1	2	20	2	5	2	2	4	1	9	2	2	0	2	3	2		
Degree 5	0	0	0	0	0	0	0	9	1	0	0	1	3	0	15	0	1	0	0	4	0		
Total of cases	54	3	5	2	9	10	16	67	17	23	6	9	16	22	32	7	7	3	3	10	9		
Mean degree of dural tension	2.44	1.66	2.00	1.00	2.22	2.40	1.87	3.25	2.64	2.74	2.83	2.77	3.25	1.82	4.09	2.57	3.29	2.67	3.33	4.00	1.78		

Absolute numbers for figure 5.
Treatments are: CSF drainage; Osmotic dehydration (Osm.); Hypotension (Hypots.); Hyperventilation (I.P.P.R.); Hypothermia (Hypothr.); Multiple methods (M.M.).

Comparison between untreated and treated patients (all treatments grouped together):
for Class I $\chi^2 = 8.53$; P between $0.05 > P > 0.02$
for Classes II + III $\chi^2 = 15.07$; P between $0.01 > P > 0.001$
for Classes IV + V $\chi^2 = 13.93$; P between $0.01 > P > 0.001$

Comparison between averages, in untreated patients, patients receiving a single treatment (CSF dr., or Hypots., or Osm., or I.P.P.R.) grouped together, and patients receiving multiple treatments:

between untreated and receiving a single treatment
for Class I $t = 2.43$; P between $0.02 > P > 0.01$.
for Classes II + III $t = 2.78$; P between $0.01 > P > 0.001$.
for Classes IV + V $t = 3.74$; $P < 0.001$.

between single treatments and multiple treatments
for Class I $t = 0.25$; $P > 0.8$.
for Classes II + III $t = 4.02$; $P < 0.001$.
for Classes IV + V $t = 2.59$; P between $0.02 > P > 0.01$.

of tense or abnormally tense duras decreased, while higher proportions of patients showed more favourable operating fields (see also table IB). The effect was irregularly distributed in the five classes, so that the correlation between dural and intracranial pre-operative tension, though still significant was less evident ($r=0.28$, $P<0.05$).

In order to facilitate further comparisons of data the five classes of intracranial condition were reduced to three, grouping together the cases belonging to classes II and III (slight or no rise in intracranial tension) and to classes IV and V (severe elevation of intracranial tension, with or without coma). Class I, obviously, did not change. In the three enlarged classes so obtained, a significant difference was found in the distribution of the different degrees of dural tension between the treated and untreated cases (table V). In table V and in figure 5, controls, single and multiple treatments were also compared. In each class no difference was demonstrable between the averages of dural tension in the controls and in the patients subjected to hypothermia alone, while a highly significant difference was evident between the same controls and the patients subjected to cerebrospinal fluid drainage, osmotic dehydration, hypotension or artificial hyperventilation. The results obtained with each of these treatments appeared roughly similar. However, no comparison was attempted between the averages, as the various procedures had not been allotted at random but chosen following precise indications, which will be discussed later.

In classes II + III and IV + V multiple treatments were significantly more successful than single treatments. In class I, where the percentage of tense duras was already very low, the difference did not reach a level of statistical significance.

The efficacy of treatments was also tested when the dura had been exposed and found to be hypertensive, or when the operating field, after opening of the dura, appeared to be unsatisfactory. In these instances, however, only a rough evaluation could be made, too many variables being involved in each case (table VI). Ventricular tap or spinal drainage was immediately effective in lowering dural tension or brain volume in about 90 per cent of cases. The favourable effect of I.P.P.R. was slower in onset (3 to 5 minutes), less evident but equally constant, even in patients where other methods had failed. Sucrose and urea were seldom used at this stage of operation. Their effect was good, fairly reliable but delayed for at least 15 to 20 minutes. Controlled hypotension failed when the abnormal dural tension was due to internal hydrocephalus or cystic tumours, and was moderately useful in the other cases.

TABLE VI

Efficacy of treatments during the course of operation.

Treatment	Successful cases	Unsuccessful cases	Total
CSF drainage	92	6	98
Controlled hypotension	16	3	19
Osmotic dehydration	12	2	14
Artificial hyperventilation	12	1	13

DISCUSSION

The method of evaluation of dural tension adopted in this study has the sole advantage of practical simplicity. It is appreciated that it is open to criticism because it is based on subjective estimations which vary from one surgeon to another and because it does not take into account the various components of intracranial tension and its causes.

In the intracranial cavity three components of the central nervous system are known to be susceptible to increase in volume as a result of pathological changes or following treatment. These are (fig. 6): the parenchymal component, comprising nervous tissue with its enveloping and supporting structures and any pathological process originating from or lying within these structures; the vascular bed with its arterial, venous and capillary components; and the cerebrospinal fluid contained in the ventricles, cisternae and subarachnoid spaces. Increases in volume and consequently in pressure may arise in the parenchymal component as a result of cerebral enlargement or oedema and/or of space-occupying lesions. The variations encountered in the circulatory field are of a strictly functional nature and may be defined, according to the

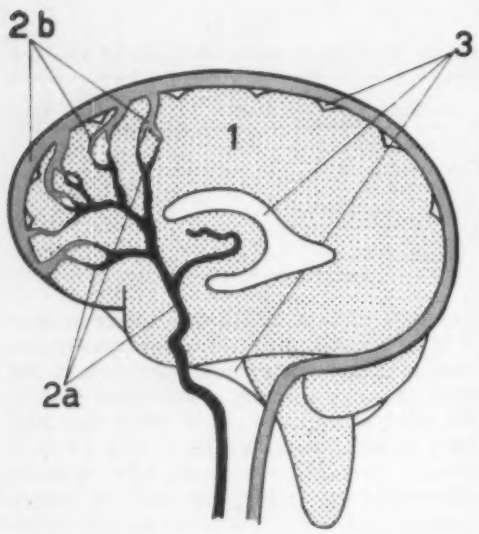

FIG. 6

Schematic representation of contents of the skull, showing areas susceptible to variation in volume.
1—parenchymal area.
2—vascular area: (*a*) arterial, (*b*) venous.
3—cerebrospinal fluid spaces (ventricles, cisternae, subarachnoid spaces).

theory of Rich, Scheinberg and Belle (1953), as variations in the "volume of vascular structures of the brain." This volume may increase either by vasodilatation and arterial hypertension or because of an impediment to the venous return from the cerebral system to the heart (Ryder, et al., 1951, 1952a, b, c). These variations may occur with great rapidity and are equally rapidly reversible. The volume of the cerebrospinal fluid may be increased by the presence of obstructions (of a neoplastic or inflammatory nature) to the normal circulation and, in general, by pathological processes which modify the equilibrium between its production and reabsorption. With regard to variations in cerebrospinal fluid volume of a physiological character, which are those of the greatest interest to the anaesthetist, though definite proof of this is lacking according to Foley (1957) and Boyd (1958), it is possible that they may arise from the same causes and vary in the same direction as those of the cerebral blood volume though much more slowly than the above-mentioned haemodynamic disturbances. It follows that changes in the volume of the cerebrospinal fluid tend to prolong the duration of the effect on the intracranial tension of circulatory modifications which have lasted more than a few minutes.

The methods at present available for the control of the intracranial tension during operations act on these three components and all tend to reduce their volume. At the moment of opening of the theca, therefore, the conditions in the operating field are the result of the interaction of multiple and diverse factors acting in opposite ways upon the volume of the intracranial structures. A brief analysis of the possible factors which could have an adverse influence on the surgical field in craniotomy has demonstrated a clear and constant relationship between the nature and seriousness of the preoperative intracranial condition and the degree of tension of the exposed dura mater. This is a logical and expected finding and no comment seems required to elucidate it. At present, a careful assessment of every available pre-operative sign of raised intracranial tension is used as a guide to the qualitative and quantitative choice of the therapeutic method.

By contrast, the influence of the type of general anaesthesia, of spontaneous variations in pulmonary ventilation and of posture appeared to be negligible. It is a matter for conjecture why general anaesthesia or certain anaesthetic agents have for long been considered unsatisfactory in the field of cerebral surgery. Cathelin (1954), for example, stated that general anaesthesia increases intracranial pressure. Woringer (1954), whilst maintaining that this is incorrect, was of the opinion that some anaesthetic agents, such as ether, should be absolutely contraindicated because of their direct effect in raising intracranial tension. It is considered that the explanation may be found in the unmistakable influence of respiration on dural tension and in the fact that the significance of the respiratory alterations caused by general anaesthesia has only recently been recognized. For some considerable time it has been known that the tension of carbon dioxide in arterial blood is by far the most important of the factors affecting the cerebral circulation and that hypoventilation

considerably increases the volume of the encephalic vascular component. Hypoxia and, still more, hypercapnia cause cerebral vasodilatation and arterial hypertension, with a consequent increase in the cerebral blood flow and in the intracranial blood volume. Moreover, in the event of respiratory obstruction, especially during the expiratory phase, a mechanical effect on the venous side of the cerebral circulation is added to this biochemical mechanism.

The data here presented suggest a correlation between the alveolar ventilation rate and the degree of dural tension but it was rather disappointing to find that the relationship was not as close as might be expected on physiological grounds. This was especially true for the narrow range of values of spontaneous ventilation recorded. At the extremes (controlled hyperventilation or single exceptional cases of severe respiratory impairment) the relationship was very impressive.

Closely concerned with the problem of the interrelated influences of respiration, venous pressures and dural tension, is that of the effect of the position of the patient on the conditions of the intracranial operative field. The advantage of the so-called "postural drainage" is well recognized but the extent to which it actually contributes towards the control of brain tension during operation has not so far been determined. In this study even the extremes of position (prone or sitting up) had, unexpectedly, no significant influence. In a few patients an increased dural tension with cerebral congestion and troublesome venous bleeding was noted which quickly subsided following correction of a faulty position of the head or neck, or of a partial respiratory obstruction. It is emphasized that the utmost care was taken to ensure good venous drainage from the skull and free respiration in every position, particularly in those which are less favourable such as, for example, the prone or when there is forced rotation or flexion of the neck. It seems that, when these two conditions are carefully fulfilled, no important advantage can be gained by further efforts to increase postural drainage.

As can be seen from table VII, a rough chronological order has been followed in this clinic in the employment of the various methods adopted to reduce brain or dural tension. As new, safer or more reliable methods appeared, the less satisfactory ones were discarded or used only when required for other indications. It is stressed, however, that during this period, the population of patients did not vary appreciably, nor did the surgical or anaesthetic techniques employed; so that, even if the management did not follow any precise experimental scheme, the results discussed here were not biased by errors such as the selection of cases or changes in the basic techniques. It is believed that the wide and significant decrease observed in the proportion of tense or hypertensive duras in the treated cases as compared with the controls, can be ascribed solely to the favourable effect of the various therapeutic methods adopted. The relative efficacy of individual treatment could be assessed only on clinical grounds. Indeed, no statistical comparison between them was permissible, because they were not allotted to each patient at random but were

TABLE VII

Chronological distribution of treatments.

	Applied before exposure of the dura							Applied after exposure or opening of the dura*					
Period	None	CSF dr.	Hypots.	Osm.	I.P.P.R.	Hypothr.	M.M.	None	CSF dr.	Hypots.	Osm.	I.P.P.R.	M.M.
1958 and before	69	14	10	0	1	13	1	71	28	6	1	1	1
Jan.–June 1959	55	10	0	0	2	13	11	56	27	5	0	0	3
July–Dec. 1959	24	2	1	11	7	6	15	34	19	1	6	0	6
Jan.–June 1960	5	1	0	24	11	4	20	42	11	2	3	4	3
Total of cases	153	27	11	35	21	36	47	203	85	14	10	5	13

* Without regard to efficacy.

employed on the basis of well defined criteria. The general method adhered to was that of dealing with the component (parenchyma, vascular bed or cerebrospinal fluid) which appeared to be chiefly responsible for the raised intracranial tension. In practice, the following procedures were adopted. In cases of large solid or cystic supratentorial tumours with perifocal oedema, hypertonic solutions were injected and/or pathological cavities were emptied. In cases of highly vascular tumours and in plethoric, congested and obese patients with respiratory insufficiency, artificial hyperventilation was preferred, sometimes in combination with hypotension and/or controlled hypothermia. In patients affected with hydrocephalus and in particular subtentorial tumours, as well as those with a transitory increase in cerebrospinal fluid pressure due, for example, to errors or difficulties in the anaesthetic management or preoperative ventriculography, the cerebrospinal fluid was drained from the ventricles, cisternae or by lumbar puncture according to the patient. This last method, which was the most commonly used in the past, is now rarely employed.

Hypertonic solutions, injected into the blood stream for the purpose of removing water from the tissues and possibly reducing the production of cerebrospinal fluid by osmosis, are well-known therapeutic devices in neurosurgery. In recent years, after discarding electrolyte and glucose solutions, whose action proved too transitory, the intravenous injection of 30 per cent solutions of urea, in a dose of 100 to 1500 mg/kg body weight, was recommended by Javid (1958), Stubbs, and Pennybacker (1960) and others. The use of 50 per cent sucrose, in doses of 200 to 300 ml was described by Ballantine and Jackson (1960). In this experiment the prophylactic use of both these solutions has proved helpful in obtaining a good operative field.

Care was taken to commence the intravenous infusion as soon as possible after the induction of anaesthesia, so that it should be completed 15 to 30 minutes before the opening of the theca. Osmotic dehydration was also successful when an actual "retraction" of the brain was desired in order to facilitate the exposure of deep structures. No untoward side effects or reactions were observed with this type of therapy. The increasing use of osmotic diuretics has led, in the authors' cases, to a reduction in the number of indications for lumbar or ventricular drainage of the cerebrospinal fluid. The slow and gradual dehydration of nervous tissue obtained with hypertonic urea or sucrose seemed preferable to the uncontrollable shift in intracranial pressure which follows the sudden emptying of ventricles or subarachnoid spaces.

The great influence of respiratory changes on the tension of the brain and on the efficacy of the various therapies has been repeatedly stressed. Quite recently Delègue et al. (1957) in France and Lundberg, Kjallquist and Bien (1959) in Sweden have shown that a reduction in the carbon dioxide tension in arterial blood, induced by hyperventilation is accompanied by a fall in intracranial tension. They consider that artificial hyperventilation is a simple and innocuous method of improving operating conditions. This method has been used as a preventative and emergency measure, when the theca or dura mater was already open, and gave satisfactory results in most patients. On the other hand, as was to be expected, only moderately satisfactory results were obtained by the use of pharmacological stimulation of spontaneous respiration. In the less severe cases this reduced an excessively high carbon dioxide tension almost to normal, though not to a condition of hypocarbia. In the patients described, artificial ventilation was effected either manually with only positive intermittent pressure or, more often, by means of a mechanical respirator using a subatmospheric phase. The results were almost identical. This is emphasized because some authors, including Ressel (1958) and Drube, Anshutz and Seusing (1958) have suggested that controlled respiration in neurosurgery is only permissible when an automatic respirator capable of providing a subatmospheric phase is used. They suggest this because they believe that positive pressure respiration results in an undesirable increase in venous and cerebrospinal fluid tension. The writers believe, in agreement with Lundberg, Kjallquist and Bien (1959), that the biochemical effects of hyperventilation prevail over the mechanical effects, in other words that the marked vasoconstriction resulting from hypocapnia more than counterbalances the possible obstacle to the venous flow.

It has been found that the observation of the

characteristics of spontaneous respiration during the various stages of operation is an invaluable guide to the patient's reaction to surgical trauma. The question, therefore, arises whether there is any justification for abolishing this valuable source of information solely in order to improve the operating field and, if so, to what extent and in which patients. It is only by considering the various factors in each individual patient that an answer to this query can be found; but the systematic and indiscriminate use of controlled respiration in all intracranial operations is definitely inadvisable. This method, however, seems to be primarily indicated in all patients showing even slight respiratory depression and, in general, in patients in whom the vascular component of encephalic tension predominates. It is found that respiratory depression is more frequent than is commonly realized.

The indications for controlled hypotension appear now to be fewer and more debatable. Whereas in 1953 this technique was adopted in more than 50 per cent of patients, often with the sole aim of achieving hypotension of the brain (Bozza, 1954), during the years 1958 and 1959 it was used in less than 10 per cent of intracranial cases. Its declining popularity is due to the greater knowledge now available concerning the factors controlling the cerebral circulation. A reduction in the blood flow and hence brain volume can be obtained by hyperventilation or, in the case of highly vascular tumours, by induced hypothermia. With neither of these techniques is the patient exposed to the serious risk of cerebral hypoxia, as may be the case when ganglion blocking drugs are used particularly if the theca is still closed (Bozza, 1954). According to Lundberg, Kjallquist and Bien (1959), cerebral vasoconstriction produced by hyperventilation never reaches a dangerous degree because there is a regulating safety mechanism which limits the diminution in the flow before hypoxia can occur. In the case of hypothermia, the reduction in the blood flow takes place at about the same rate as the decrease in the consumption of oxygen by the brain. From a theoretical point of view, controlled hypothermia seems to be an efficient means for the control of intracranial tension. It is associated with a considerable reduction in the cerebral blood flow and in the volume of the brain (Siemons and Bernsmeier, 1954; Rosomoff and Gilbert, 1955). It has been found by the writers, however, that hypothermia alone is not very helpful. On the other hand, it is felt that there is no justification, in view of the efficacy and harmlessness of other methods, for resorting to such a complex and risky technique solely in order to control the tension of the brain.

As regards certain drugs to which the function of control of the cerebral circulation has been attributed (chlorpromazine and Hydergine), experience up to date justifies rejection of this belief, though their usefulness is not denied as accessories in certain special cases.

The various procedures were often used concurrently, either in patients in whom it was essential to obtain an actual "retraction" of the brain in order to enable deep-seated structures to be operated upon, or in patients with grossly raised intracranial tension and coma.

The results more than fulfilled expectations (fig. 5 and table V), so that it is now believed that, no matter how severe the pre-operative condition, good control of brain tension during operation can be assured in almost every patient undergoing craniotomy.

The effects of two or more procedures acting on at least two of the components of intracranial tension seemed to be much more than additive, as if there was a limit to the efficacy of a single treatment which could be overcome easily by the concurrent action of a second one with a different point of attack.

SUMMARY

The factors that influence dural and brain tension, at operation, were studied in 330 patients subjected to craniotomy under general anaesthesia. The presence and seriousness of a raised intracranial syndrome prior to operation appeared to be strictly correlated with the degree of dural tension found at the opening of the theca.

Provided that the general principles of correct management of the neurosurgical patient were strictly adhered to, the type of general anaesthesia, the position of the patient on the operating table and minor variations in pulmonary ventilation were found to have a negligible influence.

The procedures which could be employed in order to reduce dural and brain tension were classi-

fied on the basis of their site of action on the three components of intracranial tension (parenchyma, vascular area, cerebrospinal fluid).

Osmotic dehydration, artificial hyperventilation, controlled hypotension and cerebrospinal fluid drainage from ventricles or lumbar subarachnoid spaces, all gave satisfactory and similar results, provided that the indications for their use were carefully selected. The safety and ease of handling of the first two procedures are stressed.

The best results were obtained when two or more procedures with a different point of attack were used concurrently.

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MUSCLE PAINS AFTER SUXAMETHONIUM AND SUXETHONIUM

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THE search for a means to prevent suxamethonium "after-pains" has been extensive and, by and large, unsuccessful (Churchill-Davidson, 1954; Hegarty, 1956; Morris and Dunne, 1957; Prince-White, 1957; Foster, 1960; Burtles and Tunstall, 1961). The use of preliminary doses of non-depolarizing relaxants appears to have been the most successful but may be followed by respiratory difficulties (Hodges, 1957; Foster, 1960).

Enderby (1959) suggested a new approach to the problem by using suxethonium bromide instead and he claimed a striking reduction in the "after-pains" incidence, as measured by spontaneous complaints made by the patients to him. However, Parbrook and Pierce (1960) have carried out a comparison between suxamethonium and suxethonium in which any complaint of pain made by the patients was noted by the ward sister, who did not know which drugs had been used. The patients were not directly questioned, so that any complaint of pain was spontaneous. The pain incidence after the two drugs was very similar.

This communication describes a trial carried out at the hospital utilizing the double blind technique and direct enquiry.

METHOD

Two hundred unlabelled 2-ml ampoules were obtained, half containing suxamethonium bromide 100 mg (equivalent to 67 mg of the chloride salt) and half suxethonium bromide 150 mg. The ampoules were labelled 1 to 200 and boxed in sixes, each box containing ampoules of the same drug. The drugs were distributed in a random fashion between the thirty-four boxes (each of six ampoules). Although the ampoule numbers in any one box were consecutive, it did not follow that the preceding or following groups of numbers were on ampoules containing the same drug. This device was adopted to ensure that if repeat doses were necessary, as for example during bronchoscopy, ampoules containing the same drug would be to hand. The anaesthetic room sister had a list of the box numbers so that continuity of drug as between boxes could also be maintained. The boxed ampoules were stored in a refrigerator prior to issue to the anaesthetic rooms. The code was held by the chief pharmacist and was not divulged until the end of the trial.

The patients, who were all to have elective surgery, were unselected except for the fact that they all required intubation (or bronchoscopy) and, except in ten instances, spontaneous respiration was allowed to return. The anaesthetic procedures were for endoscopic examinations, ear, nose, throat, plastic, dental, breast and varicose vein surgery. There were fifteen intra-abdominal operations, in five of whom spontaneous respiration was allowed to return. In the other ten d-tubocurarine was also administered and respiration controlled. Eleven of these fifteen fell into the suxamethonium group. All the hospital anaesthetists took part and the choice and dose of premedicant and anaesthetic drugs were uncontrolled. Anaesthesia was induced with thiopentone, the contents of the ampoule usually being given immediately after. The patient's lungs were then ventilated with oxygen and endotracheal intubation was carried out. Anaesthesia was continued with a nitrous oxide and oxygen mixture and a volatile anaesthetic, usually halothane. Some patients were given the ampoule contents and intubated only after they had breathed the gaseous anaesthetic for some minutes. The patient's name, age, sex, ward, the code number of the ampoule used and the drugs given, but not the dose, were entered by the anaesthetist on a special record. The patients were subsequently interviewed by the

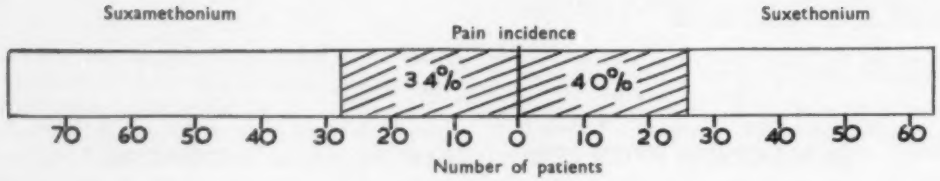

FIG. 1

To show the overall pain incidence after the two drugs.

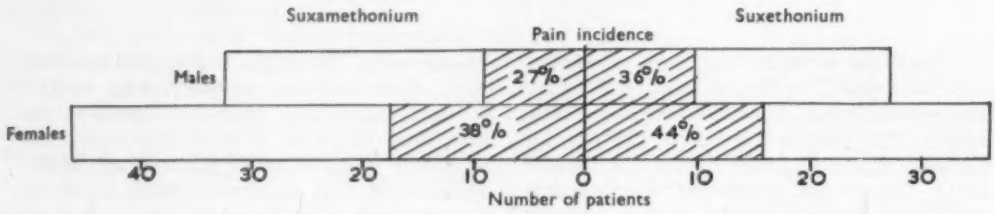

FIG. 2

To show the pain incidence after the two drugs in males and females.

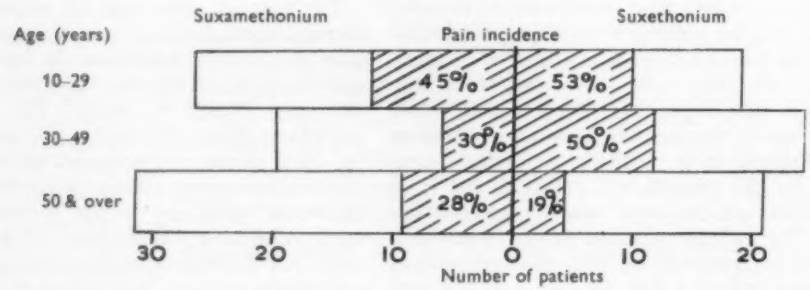

FIG. 3

To show the pain incidence after the two drugs by age groups.

TABLE I

Showing the relationship between development of pains and first getting up after administration of suxamethonium and suxethonium.

First up on	Pains developed on				No pains	Pain incidence (per cent)
	1st day	2nd day	3rd day	Subsequently		
Suxamethonium						
1st day	12	2	–	–	23	38
2nd day	4	2	–	–	9	40
3rd day	2	–	–	–	2	50
Subsequently	4	1	–	–	18	22
Suxethonium						
1st day	11	4	1	–	15	52
2nd day	5	–	1	–	10	38
3rd day	–	1	–	–	3	25
Subsequently	1	2	–	–	10	23

author at about 24 hours and again between 48 and 72 hours after operation. Enquiry was made into sickness, sore throat and aches and pains elsewhere than at the operation site.

RESULTS

Six patients in the suxamethonium group each received the contents of two ampoules. Thirteen patients in the suxethonium group received two each, and one patient received three ampoules. Thirty-six ampoules were lost to the trial by breakage or because the patient was not interviewed, mostly due to early discharge from hospital. There remained 143 patients who received the contents of 164 ampoules. The reason for using more than one ampoule was usually to obtain more prolonged relaxation, as for example, during oesophagoscopy, but of the sixty-four patients in the suxethonium group, ten were given a second ampoule because of inadequate relaxation for intubation.

The overall incidence of pains in the suxamethonium group of seventy-nine patients was 34 per cent and 40 per cent in the sixty-four patients who received suxethonium (fig. 1). As was to be expected, there was a higher incidence of pains among females in both groups (fig. 2) and both groups showed a decrease in the incidence of pains in those over 50 years of age (fig. 3). There was a decreasing frequency of pains amongst patients whose first getting up was delayed (table I).

DISCUSSION

The proportion of females was similar in the two main groups but in the suxamethonium group there was a larger number of older people, mostly female, and a greater percentage did not get up till after the third postoperative day. These three factors may account for the lower incidence of pains in this group. But the incidence is much lower than that reported for a study (Burtles and Tunstall, 1961—suxamethonium control group 49 per cent pain) carried out under very similar circumstances. A possible explanation is that in the earlier study stock supplies of Scoline brand of suxamethonium chloride were used, whereas in this investigation special ampoules of Brevidil M brand of suxamethonium bromide were used and they were kept refrigerated until not more than 10 days prior to use. Against this must be set the fact that Leatherdale et al. (1959) used stock Scoline and freshly prepared Brevidil M and were unable to demonstrate any difference in the pain incidence. Enderby (1959) also used stock supplies of Scoline.

No patient in either group was classified as having "severe" pains according to Hegarty's (1956) classification and there were only seven who came into the "moderate" group (four being in the suxamethonium series). In all but two of these the pains were very mild but were felt in more than one site.

Enderby reported that spontaneous complaints of pain were made to him in 17 per cent of the patients in his suxamethonium series but in only 4 per cent of patients in the suxethonium group. In a second study, in which he employed direct enquiry, the incidence rose to 50 per cent and 34 per cent respectively, suggesting that the suxethonium pains are milder. Although Parbrook and Pierce (1960) did not use direct enquiry, the ward sister concerned would certainly hear of complaints of muscular stiffness that the patient might well consider too minor to mention to a visiting doctor, especially if he was one to whom they were indebted. For this reason alone the results in Enderby's first series and Parbrook and Pierce's study are probably not comparable. It must be noted that Enderby's patients also received decamethonium which might be thought to lead to a higher frequency of pains since the use of this drug alone can produce "after-pains". However, Hegarty (1956) found a reduced pain incidence after the use of decamethonium and suxamethonium (12.7 per cent) as compared with suxamethonium alone (25.6 per cent) and it may be that this effect is more pronounced with suxethonium.

The paralyzing action of the dose (150 mg) of suxethonium used in the present study appears to be both brief and often incomplete and experience is in accord with the description given by Parbrook and Pierce, although they used a dose of 180 mg.

In twenty-two patients, the interval between the administration of thiopentone and of the relaxant was recorded as being 4 minutes or more (fig. 4). Thirteen of these patients had received suxamethonium and nine complained of pains;

of the remaining nine patients who had been given suxethonium eight complained of pains (two in the former group and one in the latter group being classed as "moderate"). This pain incidence is very much higher than in the whole series and lends support to the suggestion (Burtles and Tunstall, 1961) that thiopentone exerts some protective influence in this respect.

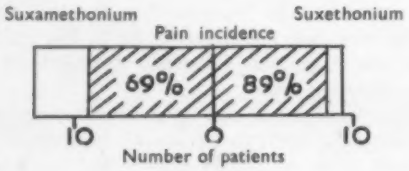

FIG. 4

To show the overall pain incidence when the drugs were given 4 minutes or more after the thiopentone.

CONCLUSIONS AND SUMMARY

Under the conditions of this experiment it appears that the pain producing properties of suxethonium are similar to those of suxamethonium. In view of this and the inconsistencies of the action of suxethonium, there are no grounds for recommending the abandonment of suxamethonium. It is suggested rather that its use be restricted to those patients in whom the advantages of rapid and complete paralysis outweigh any disadvantages, such as prolonged muscle stiffness.

ACKNOWLEDGMENTS

I should like to express thanks to Dr. O. P. Dinnick for much helpful criticism, to the entire anaesthetic staff for their co-operation, to Mr. G. Bryan, chief pharmacist, for preparing the labelling and boxing of the ampoules, and to Messrs. May & Baker for preparing the special ampoules of Brevidil M and E.

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MUSCLE PAINS AFTER SUXAMETHONIUM CHLORIDE IN CHILDREN

BY

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SOON after the introduction of suxamethonium chloride into clinical practice it was noticed that some patients who had received this drug developed muscle pains postoperatively (Bourne Collier and Somers, 1952; Churchill-Davidson, 1954). Since then many reports have dealt with the incidence of muscle pains in adults but there has been little interest in this complication in children. Ruddell (1959) states that he has never seen it in a child, and Foster (1960) comments on the lack of occurrence of muscle pains in children. In order to put this clinical impression to the test it was decided to determine the incidence of muscle pains occurring postoperatively in children who had received an intravenous injection of suxamethonium chloride.

METHOD

The investigation was confined to inpatients and was limited to those children who were ambulant on the day after operation. Because of this limitation only those patients who underwent the following operations were included: ear, nose and throat operations such as tonsillectomy, adenoidectomy, antrum washouts and nasal polypectomy; manipulation and splinting of fractures of the upper limb; and minor lacerations.

The anaesthetic technique used in these patients was as follows. Pre-operative medication was not standardized and consisted of either pethidine 5 mg/stone (0.8 mg/kg) body weight or morphine 1/40 grain (1.5 mg/stone; 0.25 mg/kg) body weight together with atropine 1/100 grain (0.6 mg) with or without trimeprazine 30 mg or atropine 1/100 grain (0.6 mg) alone. The influence of premedication on postoperative muscle pains will be discussed later.

Anaesthesia was induced in all patients using a standard dose of thiopentone 25 mg/stone (4 mg/kg) body weight. Suxamethonium chloride, in a standard dose of 10 mg/stone (1.6 mg/kg) body weight, was injected rapidly through the same needle. The patient's lungs were inflated with a nitrous oxide and oxygen mixture, and the occurrence and severity of muscle fasciculations were noted. Muscle fasciculations were graded into two groups; in the mild group fasciculations were of brief duration and only fine movements were observed, whilst in the severe group fasciculations were of longer duration and coarse movements were observed. The child was then intubated, ventilation was controlled using a suitable anaesthetic system and intermittent doses of suxamethonium chloride were given as required.

On the morning after operation each child was interviewed by one of us (F.R.) and by then had been ambulant in the ward for about 4 hours. Before questioning the child the ward sister was asked: "Did the child spontaneously complain of pain or stiffness?" If the answer was in the affirmative this pain was classified as "severe". The child was then seen and, having obtained his cooperation, he was asked: "Have you or had you any pains or stiffness this morning?" In order to determine whether the pains and stiffness felt by the child were unrelated to the site of operation and hence were muscle pains, the child was then asked: "Where are the pains?" A positive reply to these questions was then classified as "moderate" or "mild" depending on the degree and duration of the pains. If the reply was negative the child was then directly questioned: "Have you any pains in your neck, back, chest, tummy, arms or legs?" If the answer was in the affirmative, the pains were classed as "mild".

RESULTS

Three hundred patients were observed in this investigation. The ages of the children varied from 5 to 14 years. The number of patients in each age group is shown in figure 1. The incidence of muscle pains according to the age of the patient is shown in figure 2. Whilst the overall incidence was 10 per cent, in the 5 to 9 years group the incidence was only 3 per cent compared with an incidence of 23 per cent in the 10 to 14 years group.

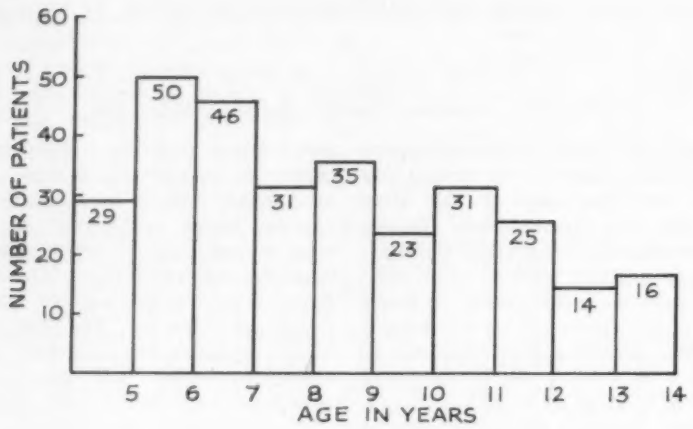

FIG. 1
Age distribution of patients

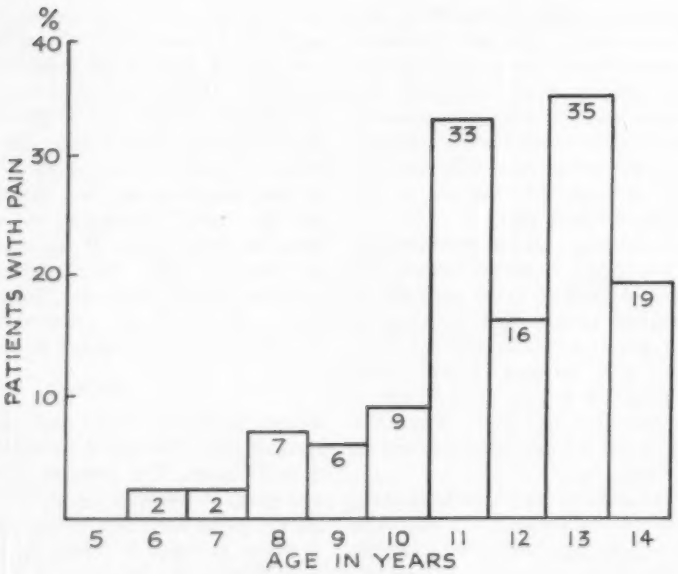

FIG. 2
Incidence of pain in relation to age.

This difference between these two age groups is statistically highly significant ($P<0.001$).*

There were 165 boys and 135 girls in the series and figure 3 shows the incidence in either sex. The observed difference of 7.5 per cent is statistically significant ($P<0.05$).

Table I shows the relationship between premedication and the occurrence of muscle pains. There is no statistical evidence that the type of premedication influenced the occurrence of postoperative muscle pains.

The relation between the severity of muscular fasciculations and muscle pains is shown in tables II and III. There is obviously no correlation. Since the occurrence of fasciculations in the older age group (71 per cent) is significantly higher ($P<0.01$) than in the younger age group (53 per cent *v.* fig. 4) and since older children have a greater incidence of postoperative muscle pains it might be imagined that there could be a

*The results were evaluated using the chi-square test.

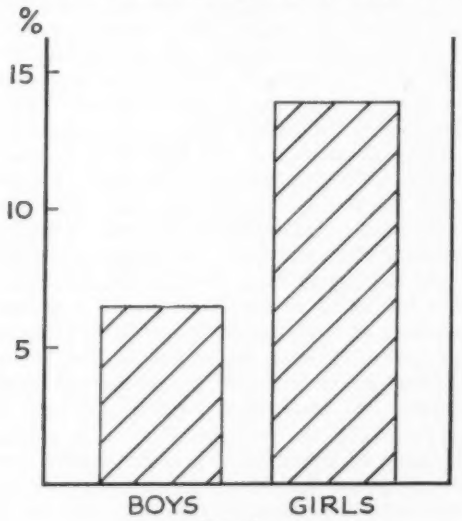

FIG. 3
Incidence of muscle pains in either sex.

TABLE I
Analysis of results in relation to premedication.

Premedication	Total no. children	With pain	
		No.	Percentage
Methotrimeprazine Pethidine Atropine	72	6	9
Methotrimeprazine Morphine Atropine	32	5	15
Pethidine Atropine	21	2	10
Morphine Atropine	67	7	10
Atropine only	108	10	9

TABLE II
Showing relation between fasciculations and pain in age group 5 to 9 years.

Pains	Fasciculations			
	Moderate	Mild	Nil	Total
Severe	–	–	–	–
Moderate	–	–	–	–
Mild	–	3	3	6
Nil	18	82	84	185
Total	18	85	88	191

TABLE III
Showing relation between fasciculations and pain in age group 10 to 14 years.

Pains	Fasciculations			
	Moderate	Mild	Nil	Total
Severe	–	1	–	1
Moderate	2	7	–	9
Mild	4	6	4	14
Nil	21	36	28	85
Total	27	50	32	109

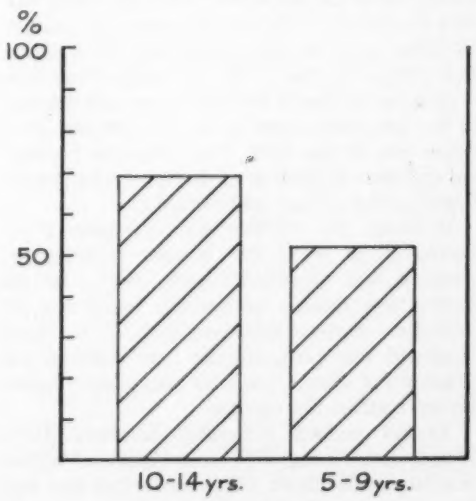

FIG. 4
Incidence of fasciculations in two age groups.

correlation between the occurrence of muscle pains and the fasciculations. However, in the older age group only 20 patients had both fasciculations and postoperative muscle pains, compared with 57 patients who only had fasciculations and no muscle pains. Similarly, in the younger age group only 3 patients had fasciculations and postoperative muscle pains, compared with 100 patients who only had fasciculations and no muscle pains. There is therefore no relation between the occurrence of fasciculations and postoperative muscle pains.

DISCUSSION

This investigation confirms the clinical impression that children suffer less frequently from postoperative muscle pains than adults. The incidence of muscle pains in adults is variously reported as 66 per cent (Churchill-Davidson, 1954), 20 to 25 per cent (Hegarty, 1956), 72 per cent (Morris and Dunn, 1957) and 36 per cent (Leatherdale, Mayhew, and Hayton-Williams, 1959). The incidence of pains in the present series was 10 per cent. Only one of the patients had pains which could be classified as severe. The onset of the pains and stiffness was usually 12 to 20 hours after operation. Those who had pains were aware of them when they woke up next morning and usually the pains disappeared rapidly. There was only one patient in whom they were still present 24 hours after suxamethonium had been given. It is interesting that in the age group from 5 to 9 years the incidence was only 3 per cent whereas in the age group from 10 to 14 years the incidence was 23 per cent. The difference between the incidence of pains in adults and children under 9 years of age is thus quite striking.

In adults the incidence among women is reported to be twice that in men (Leatherdale, Mayhew and Hayton-Williams, 1959). In the present investigation we similarly noted this sex difference between boys and girls. It has been suggested that premedication may influence the incidence of muscle pains but the present results do not confirm this opinion.

Several authors (Churchill-Davidson, 1954; Morris and Dunn, 1957; Leatherdale, Mayhew and Hayton-Williams, 1959) have stated that they found no correlation between the occurrence of muscular fasciculations seen soon after the intravenous injection of suxamethonium and postoperative muscle pains. No correlation was observed in this investigation.

Since the cause of the postoperative muscle pains is still unknown, it is interesting to discuss the difference in the incidence of these pains in the adult and younger child. Paton (1959) discusses the various theories as to their causation. Where it is believed that the fasciculations do have some relationship to the postoperative muscle pains, the mechanism of the production of the fasciculations has been explained as being due to either an axon reflex (Masland and Wigton, 1940) or activation of the gamma fibre system (Paton, 1959). Where it is thought that the pains and fasciculations are not directly related, the pain could be explained on the basis of the development of a "contracture". In both cases the pains are thought to be due to muscle damage occurring during the fasciculations or "contracture".

One explanation of the difference between adults and children could be that there is a more rapid circulation in children. In this case fasciculations would rapidly give way to neuromuscular block and hence the degree of trauma would be reduced (Rees, 1960). In this connection it is interesting to note that there is a greater incidence of fasciculations in the 10 to 14 years age group. Another explanation is that young children are more active than adults and older children and hence more supple. This view is supported by the fact that there is a greater incidence of muscle pains in older children and also a greater incidence in girls, who may be expected to be less active than boys. One factor that must be borne in mind is the clinical impression that younger children have less appreciation of pain than their older colleagues. Despite the difficulty in obtaining unbiased information from younger children, it is believed that the present results are as accurate as possible.

It has been advocated (Morris and Dunn, 1957) that suxamethonium should not be used in adults who are ambulant soon after operation, because of the high incidence of postoperative muscle pains. Because of the extremely low incidence of these muscle pains in younger children, there can be no valid objections on these grounds to the use of suxamethonium in this age group. Even in children of the older age group, the incidence,

severity, duration, and incapacity caused by muscle pains is significantly less than in adults.

SUMMARY

An investigation was carried out to determine the incidence of muscle pains following the use of suxamethonium intravenously in children from 5 to 14 years old. The overall incidence was 10 per cent, although in the group between 5 and 9 years old the incidence was only 3 per cent. There was a significant difference in incidence between boys and girls. No correlation between the incidence of muscle fasciculations and postoperative pains could be found. Possible reasons for the different incidence of muscle pains in children and adults are discussed. It is suggested that there are no valid objections on these grounds to the use of suxamethonium in children of the younger age group.

ACKNOWLEDGMENTS

We are grateful to Dr. G. J. Rees who originally suggested this investigation and for his help and guidance in the preparation of this paper. Our thanks are also due to the other members of the Department of Anaesthesia of Alder Hey Children's Hospital, in particular to Dr. A. L. Stead and to the ward sisters for their help and co-operation throughout this investigation.

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THE EFFECT OF HALOTHANE ON THE NEWBORN INFANT DELIVERED BY CAESAREAN SECTION

BY

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SINCE the introduction of halothane into clinical practice (Johnstone, 1956; Bryce-Smith and O'Brien, 1956; Brennan, Hunter and Johnstone, 1957) it has been used to an increasing extent as an anaesthetic agent throughout Britain and North America. Inevitably it has been employed in obstetrical work, especially for Caesarean section where its potency, flexibility and non-irritant properties offer immediate advantages. The purpose of the present investigation was to ascertain by comparative methods the effect of halothane anaesthesia during Caesarean section on the newborn infant.

Assessment of the condition of babies at birth has been unsatisfactory in the past because the criteria of different workers have not been similar. The system introduced by Apgar (1953), and employed in this investigation, is receiving wide recognition and is such that comparable results should be obtainable by other workers—obviously desirable if further knowledge is to be gained in this field.

METHOD

A comparison was made using the Apgar scoring method of the condition of infants born after Caesarean section using two anaesthetic techniques. Details were recorded of 166 operations for Caesarean section over a period of 10 months at St. Mary's Hospital, Manchester. The cases were divided into elective and emergency groups. The technique used in any individual patient was selected at random and was not influenced by the patient's condition or the reason for operation. The premedication used in all cases was atropine 0.6 mg. The first anaesthetic technique employed was a thiopentone, suxamethonium, nitrous oxide and oxygen sequence. A dose of thiopentone not exceeding 250 mg was injected intravenously to produce sleep and was followed by suxamethonium chloride 50 mg. The patient was then well oxygenated and intubated with a lubricated cuffed endotracheal tube. Anaesthesia was maintained using a nitrous oxide and oxygen mixture, with a total flowrate of at least 7 l./min in a Magill circuit. Respiration was controlled and supplementary doses of suxamethonium chloride were given when necessary. The alternative anaesthetic technique employed was a thiopentone suxamethonium, halothane, nitrous oxide and oxygen sequence. The patient was anaesthetized and intubated as in the first technique but anaesthesia was maintained with a halothane-nitrous oxide-oxygen mixture using a concentration of halothane of 1 to 2 per cent delivered from a Fluotec vaporizer in a Magill system with a total gas flow of at least 7 l./min. Spontaneous respiration was permitted. The average time interval between the induction of anaesthesia and delivery of the infant in the entire series was 23 minutes (range 9–35 min).

One minute by the clock after complete delivery of the infant from the mother the evaluation of the condition of the baby was carried out. This was performed jointly by paediatrician and anaesthetist and agreement was reached before a score was entered for a particular child. The paediatrician was unaware which anaesthetic technique was being employed. The method of evaluation followed exactly that described by Apgar (1953) and briefly consisted of the allocation of a numerical score to the child based on the observation of five physical signs. These were: heart rate; respiratory effort; muscle tone; response to the insertion of a catheter in the nostril (tested after the oropharynx had been

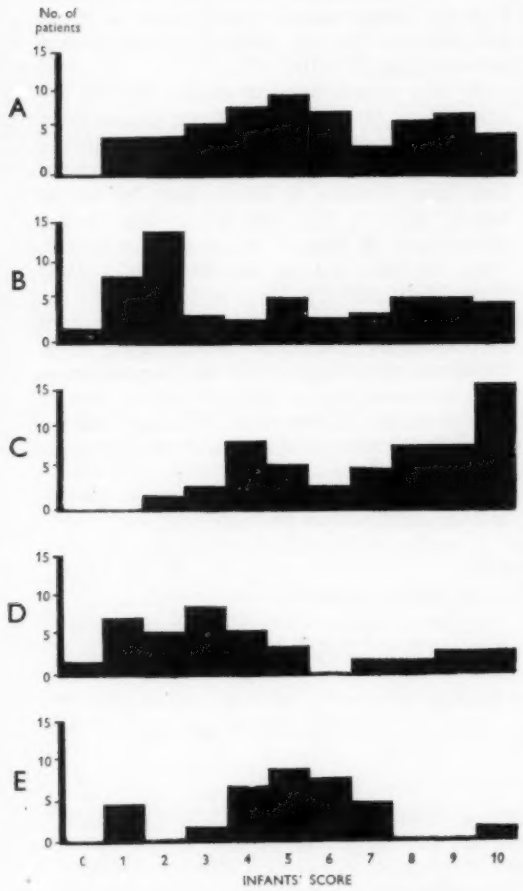

FIG. 1

A. Elective Caesarean section: distribution of infants' scores using thiopentone, suxamethonium, nitrous oxide and oxygen.

B. Elective Caesarean section: distribution of infants' scores using thiopentone, suxamethonium, halothane, nitrous oxide and oxygen.

C. Normal delivery: distribution of infants scores.

D. Emergency Caesarean section: distribution of infants' scores using thiopentone, suxamethonium, halothane, nitrous oxide and oxygen.

E. Emergency Caesarean section: distribution of infants' scores using thiopentone, suxamethonium nitrous oxide and oxygen.

cleaned); and the colour of the child. Each of these signs could be given a score of 0, 1 or 2. For example—respiratory effort: if this was absent after 60 seconds a score of 0 was recorded; if good crying was present a score of 2 was given; and if respiration was slow and irregular a score of 1 was obtained. A score of 10 for any individual infant indicated that it was in the best possible condition.

In order to obtain a basis for comparison a number of infants who had normal vaginal deliveries were evaluated. The infants were unselected and the majority of mothers received some form of pain relief during labour such as pethidine, trichloroethylene in air or nitrous oxide in air. In this group the assessment was made by a doctor who was present at delivery.

RESULTS

The numbers of infants studied in the various groups are shown in table I and the average scores obtained as shown in table II. The distribution of the results is shown in figure 1. Six tests were applied to these distributions of scores:

TABLE I

Numbers of Caesarean sections and normal deliveries.

	Total	Elective C.S.	Emergency C.S.
Thiopentone, suxamethonium, halothane with nitrous oxide and oxygen	82	49	33
Thiopentone, suxamethonium, nitrous oxide and oxygen	84	53	31
Total	166	102	64
Normal deliveries	50		

TABLE II

Average score of infants (Apgar system).

	Elective C.S.	Emergency C.S.
Thiopentone, suxamethonium, halothane with nitrous oxide and oxygen	4.7	3.8
Thiopentone, suxamethonium, nitrous oxide and oxygen	5.5	4.8
Normal deliveries	7.3	

(1) A comparison was made between the distributions of the scores obtained by infants born by elective Caesarean section using the two anaesthetic techniques. Infants born after the thiopentone, suxamethonium, nitrous oxide and oxygen technique had been employed were in better condition and this favourable distribution was shown to be significant ($P \simeq 0.03$).

(2) The results of elective Caesarean section using both techniques were combined and were then compared with the distributions obtained in infants born by normal vaginal delivery. This showed that infants born by normal vaginal delivery were in better condition and that the difference in distribution between the two sets of infants was significant ($P<0.001$).

(3) The distribution of scores obtained for infants born by elective Caesarean section using the thiopentone, suxamethonium, nitrous oxide and and oxygen sequence were compared with those obtained in infants born by normal vaginal delivery. This comparison showed that infants born by normal vaginal delivery were in better condition and that the difference in distribution was significant ($P=0.01$).

(4) The distributions of scores obtained for infants born by elective Caesarean section using the thiopentone, suxamethonium, nitrous oxide and oxygen with halothane sequence were compared with those obtained in infants born by normal vaginal delivery. This comparison showed that infants born by normal vaginal delivery were in better condition and that the difference in distribution was significant ($P<0.001$).

(5) The distribution of scores of infants born by emergency Caesarean section using both techniques was compared with the scores of infants born by normal vaginal delivery. Infants born by normal vaginal delivery were in better condition and this difference in distribution was significant ($P<0.001$).

(6) A comparison was made between the dis-

TABLE III

Evaluation of distribution of infants' scores.

	Series	No. of patients	χ^2	Degrees of freedom	Probability
Test 1	Elective C.S. Suxamethonium	53	11.03085	4	$P \simeq 0.03$
	v. Halothane	49			
Test 2	Elective C.S. Suxamethonium + Halothane	102	20.11000	4	$P < 0.001$
	v. Normal deliveries	50			
Test 3	Elective C.S. Suxamethonium	53	13.05318	4	$P=0.01$
	v. Normal deliveries	50			
Test 4	Elective C.S. Halothane	49	24.14922	4	$P < 0.001$
	v. Normal deliveries	50			
Test 5	Emergency C.S. Suxamethonium + Halothane	64	31.01871	4	$P < 0.001$
	v. Normal deliveries	50			
Test 6	Emergency C.S. Suxamethonium	31	15.65517	4	$P=0.004$
	v. Halothane	33			

TABLE IV

Numbers and causes of neonatal deaths.

	Technique	Cases		Deaths
Elective Caesarean section	Thiopentone, halothane, nitrous oxide and oxygen	49	4	1 prematurity; 1 pneumonia; 1 stillbirth; 1 haemolytic disease of the newborn
	Thiopentone, suxamethonium, nitrous oxide and oxygen	53	3	1 prematurity; 1 pneumonia; 1 haemolytic disease of the newborn
Emergency Caesarean section	Thiopentone, halothane, nitrous oxide and oxygen	33	2	1 stillbirth; 1 foetal abnormality
	Thiopentone, suxamethonium, nitrous oxide and oxygen	31	0	
Normal delivery		50	1	Prematurity

tributions of the scores obtained by infants born by emergency Caesarean section using the two techniques. Infants born after the thiopentone, suxamethonium, nitrous oxide and oxygen technique had been employed were in better condition and this favourable distribution was shown to be significant ($P = 0.004$).

These distributions were evaluated by the chi-square test. The results are shown in table III.

The neonatal deaths which occurred are shown in table IV. No neonatal death occurred which was attributable to either anaesthetic technique. There were no maternal deaths.

DISCUSSION

Hodges, Bennett, Tunstall and Knight (1959) have suggested that the thiopentone, suxamethonium, nitrous oxide with oxygen sequence is less depressant to the newborn infant than other commonly used anaesthetic techniques. They did not investigate halothane. Sheridan and Robson (1959) reported on the use of halothane in 2,583 vaginal deliveries and concluded that, provided anaesthesia was kept at a light level, undue depression of the baby should not occur. However, no Caesarean sections were included in their series and they compared halothane with a composite group of other anaesthetics including trichloroethylene, cyclopropane and regional techniques. The results in the present study show that when patients undergoing elective or emergency Caesarean section were anaesthetized using halothane in a concentration of 1 to 2 per cent as described earlier, there was more depression in the infant than was the case when the thiopentone, suxamethonium, nitrous oxide with oxygen sequence had been employed. Apgar (1953) and Apgar et al. (1957), showed that regional block in Caesarean section was greatly superior to cyclopropane in this respect and differed little from normal delivery. The scores obtained in the present series using halothane are very similar to those of Apgar (1953) using cyclopropane and there would appear to be little to choose between these agents as regards their effect on the infant. It would seem, therefore, that the thiopentone, suxamethonium, nitrous oxide and oxygen sequence is superior to both cyclopropane and halothane as an anaesthetic method for Caesarean section as regards the condition of the infant after delivery but much inferior as compared with either regional block or normal delivery. As might be expected the babies born after elective Caesarean section were more active when either technique was used than after emergency Caesarean section.

Halothane would seem to offer little advantage as an anaesthetic agent for use in Caesarean section. In addition to its greater depressant effect on the infant than other available techniques, it has a very powerful relaxant action on uterine muscle (Albert, et al., 1959; Dixon and Matheson, 1958; Embrey, Garrett and Pryer, 1958). This latter property was observed on several occasions in the author's cases after delivery and it proved impossible to obtain good uterine retraction by the normal methods until the drug had been withdrawn, after which the muscle recovered its tone with remarkable speed.

SUMMARY

A comparison has been made of the results following the use of two techniques of anaesthesia for Caesarean section. Thiopentone, suxamethonium, nitrous oxide and oxygen (artificial ventilation) caused less foetal depression than thiopentone, suxamethonium, nitrous oxide and oxygen with halothane (spontaneous respiration).

ACKNOWLEDGMENTS

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Brit. J. Anaesth. (1961), 33, 161

FLUIDS AND CHILDREN*

BY

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CHILDREN, particularly babies, present a special problem as regards fluid therapy because so large a proportion of their bodies is fluid. This relative excess of fluid, which is reciprocal with a diminution in the amount of fat, is the reason why babies are especially liable to become dehydrated rapidly. To add to the difficulties of management their circulation is more easily overloaded so that intravenous fluids must be used with even greater care than in adults. Newborn babies, particularly those born prematurely, require little or no fluid for the first 48 hours, and during recent years better survival rates have been obtained with premature babies by not feeding them for the first few days. When this regime was introduced, small babies were starved for up to 5 days but now this period has been reduced, though it is still exceptional to give any fluids for the first 12 hours, and most babies are given their first feed between 12 and 24 hours after birth.

A major problem in babies is that changes occur more rapidly than in adults and a serious clinical state which in an adult might take days to build up may in a baby take only a matter of hours. Temperature regulation is less efficient than in the adult so that wide fluctuations may occur in babies. Recently a baby was admitted with a temperature of 106°F which needed very active steps to reduce. Having lowered this to 102°F, cooling was stopped but the temperature went on falling to about 91°F and it proved necessary to put the baby into an incubator in order to bring the temperature back to a normal figure. Because of this, care must be taken to ensure that babies in an operating theatre do not get cold and a room temperature which is adequate for an adult will be too cold for a baby. It has been found particularly that babies undergoing Ramstedt's operation for pyloric stenosis fare badly if they are allowed to get cold in the theatre. Equally, of course, overheating must be avoided.

Another aspect of the difference between babies and older children or adults is their differing electrolyte balance. For example, the plasma pH of a normal baby is lower than that of an adult. Much work still remains to be done on the electrolyte values for normal premature babies and whether it is permissible to speak of a "normal" premature baby might be open to question.

This lower pH usually results from a metabolic acidosis and is therefore associated with a low plasma bicarbonate due to a rise in organic acids. However, in one seventh of premature babies the acid pH is due not to a metabolic acidosis but to a respiratory acidosis and therefore is associated with a raised bicarbonate. This means that in assessing the electrolyte state of the baby the bicarbonate, the chloride and the pH must be estimated, though unfortunately the assessment of the pH is not yet in general use. Despite this lack it is helpful to know the levels of bicarbonate, chloride, potassium, sodium and urea when taken in conjunction with the clinical picture. All electrolyte estimations are unsatisfactory because the measurement of the electrolyte level in the plasma, which only occupies 5 per cent of the total body weight, is obviously a very inadequate reflection of what is going on in the other compartments. This can be appreciated from the accompanying diagram (fig. 1).

Moreover very considerable differences exist between extracellular fluid (plasma and interstitial fluid) and intracellular fluid as shown in table I.

It should be appreciated that these figures are taken from average "normal" individuals and rigid adherence may not be valid in diseased patients. Added to this, estimations do not give a continuous picture of the electrolyte state since

*Adapted from an address to the Society of Anaesthetists of the South-Western Region on May 20, 1960.
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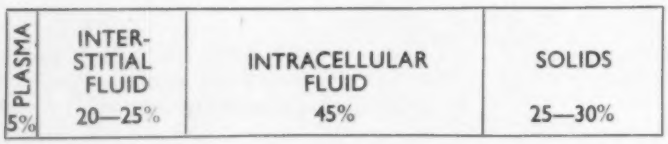

FIG. 1

Fluid and solid components of body weight in infancy. (There is some variation in these proportions with age. For the purpose of calculation the total body water is usually taken as being 70 per cent of total body weight.)

TABLE I

Body fluid constituents. (Interstitial fluid shows slight differences from plasma—in particular, the protein is only 2 m.equiv.)

PLASMA (m.equiv/l.)			
Na^+	142	HCO_3'	27
K^+	5	Cl'	103
Ca^{++}	5	Org. acids	6
Mg^{++}	3	PO_4'''	2
		SO_4''	1
		Protein	16
Total	155	Total	155

INTRACELLULAR FLUID (m.equiv/l.)			
Na^+	10	HCO_3'	10
K^+	140	HPO_4'''	100
Mg^{++}	45	SO_4''	20
		Protein	65
Total	195	Total	195

samples are taken only once, or at most twice, a day. Therefore great use must be made of the clinical assessment, particularly in regard to weight, temperature and the intake and output of fluids. In long term problems such as renal disease, it is also necessary to estimate the total daily excretion of electrolytes in the urine if the amount lost by the body is to be known.

Clinical assessment of the patient, in addition to electrolyte estimation, is vital. In babies dehydration is detected by the sunken eyes and depressed anterior fontanelle and by the loss of elasticity of the skin. In testing for elasticity the skin over the ribs should be used in preference to the abdominal skin, since in a marasmic baby a false impression of loss of elasticity may be given in the abdominal skin from loss of weight rather than loss of fluid. The dehydrated baby becomes lethargic and the cry becomes weak. In alkalosis, particularly as for example in the pyloric baby, the respirations become shallow and the cry feeble or less frequent, a state which may lead a mother to describe her baby as being "very good recently".

To understand the effect of the loss of different body fluids the normal constituents of these fluids must be known. These can best be considered in compartments (fig. 2).

Gastric juice.

The main change consequent upon a loss of gastric juice is a fall in hydrogen, chloride and sodium ions with a smaller loss of potassium. The result is hypochloraemic acidosis with hypokalaemia and the requirements for fluid therapy are sodium chloride, potassium chloride and enough 5 per cent glucose to correct the dehydration. Potassium should never be given until the baby is hydrated because of the risk of cardiac arrest from overdosage. Whenever possible potassium should be given by mouth rather than intravenously. The body can deal with excess potassium when given by mouth but excess intravenous potassium is extremely dangerous.

Intestinal juice.

The main cation in intestinal juice is sodium so that loss of intestinal juice causes a fall in water and salt. The body has excellent sodium chloride reserves but eventually the compensatory mechanisms are exhausted and the baby becomes dehydrated and acidotic. The main replacement fluid is saline, but if severe acidosis develops sodium lactate should be used as it is more effective than saline in the replacement of base.

Bile and pancreatic juice.

These can be taken together because they are constitutionally similar and are often lost together.

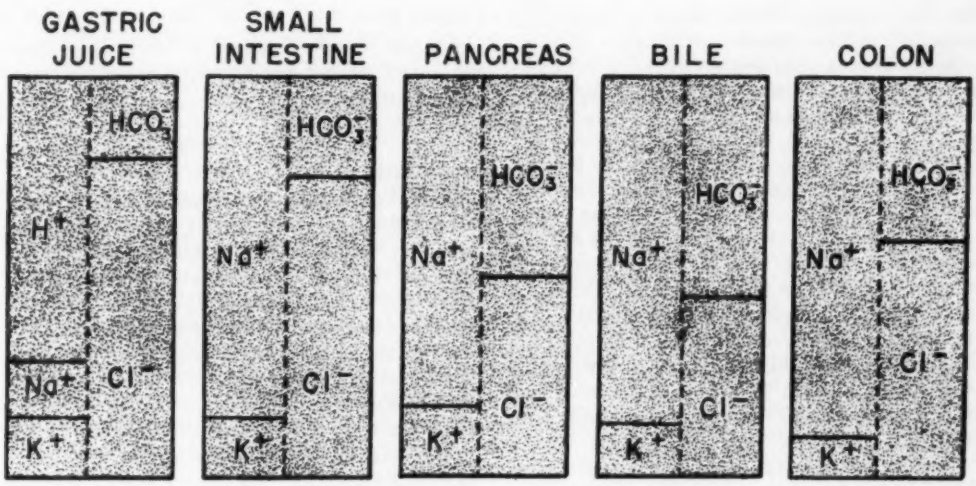

FIG. 2

Comparative electrolyte content of different body fluids.
(Reproduced from: Baffes, T. G., *Surgical Clinics of N. America*, 1956, **36**, 1453, with kind permission of the author and of the publishers of *Surgical Clinics of North America*.)

They are highly alkaline, since they contain more bicarbonate than does intestinal juice and their loss results in severe dehydration with a rapidly produced acidosis. Therefore sodium lactate should be given first followed by saline and potassium chloride.

Colon fluid.

This may occur, for example, in large-intestine diarrhoea. The loss here is mainly of a balanced solution of saline and therefore results in dehydration with secondary acidosis. If the diarrhoea is severe, shock occurs. Replacement fluid consists of saline and potassium chloride. In the home 5 per cent glucose and 1/5 normal saline can be prescribed for a baby with diarrhoea by instructing the mother to add one teaspoon of sugar and one saltspoon of salt to every 5 oz. (150 ml) of fluid. Many babies with gastroenteritis who are vomiting the boiled water that they have been prescribed will stop vomiting after being given this saline solution.

DETERMINATION OF FLUID AMOUNTS

Total fluid.

For maintenance purposes 75 ml (2½ oz.) of fluid per pound (0.45 kg) body weight in 24 hours is required. If the baby is dehydrated 90 ml/lb. is required. Newborn babies require less and 45 ml/lb. is adequate during the first week, this being increased to 75 ml by the age of 2 weeks. Premature babies require even less, the figure being 30 ml during the first week and then a proportionate increase.

Saline.

For maintenance purposes 10 ml/lb. body weight per day of normal saline are required for children of up to 50 lb. and 5 ml for children over 50 lb. This is given in the form of 1/5 N saline and 5 per cent glucose.

Correction of chloride deficit.

If the level of chloride is lower than normal it is necessary to give an additional amount of saline to supplement the maintenance saline. The amount of this additional saline is estimated from the patient's serum chloride level. The difference between the patient's figure and the normal figure of 103 m.equiv/l. gives the deficit for that child. But only 70 per cent of the body weight is fluid and therefore the total body deficit equals the serum deficit multiplied by 70/100 of the weight in kilograms. The amount of fluid to be given can be calculated from this, knowing the quantity of sodium chloride in the different solutions avail-

able. For example, normal saline contains 15.3 m.equiv/l. sodium chloride per 100 ml.

As an approximate guide, 30 ml of N saline per kilogram (15 ml/lb.) of body weight is required for the correction of moderate alkalosis.

Correction of carbon dioxide combining power.

Sodium lactate is used for the correction of a low carbon dioxide combining power and 1.8 ml of 1/6 molar sodium lactate per kilogram of body weight will raise the bicarbonate by 1 millequivalent per litre. This figure is reached because it is necessary to correct for the fact that the extracellular fluid is only 30 per cent (plasma 5 per cent and interstitial fluid 25 per cent) of the body weight (see fig. 1). Thus 30/100 multiplied by 6, since 1/6 molar sodium lactate is used, gives the figure of 1.8.

Turning now to the problem of a high carbon dioxide combining power, in the types of alkalosis usually met with in children, for example pyloric stenosis, saline is adequate to reduce the bicarbonate and the amount of saline is estimated on the basis of the chloride deficit as already described. If alkalosis is extreme, ammonium chloride may be used but this is not without risk and may cause toxic reactions including convulsions.

In all calculations an important precaution should be taken. Figures of electrolyte levels provide only an estimate of the state of the whole body and therefore only half the calculated quantity should be given in the first place. The baby is then given the maintenance fluid of 1/5N saline and 5 per cent glucose while the results are checked. Oral rather than intravenous fluids should be given if possible. Provided there is no intestinal obstruction vomiting may cease if feeds are given by drip through a gastric tube.

Protein requirements.

When a baby is on long-term intravenous therapy extra daily protein should be given in the form of plasma. Full strength plasma contains 5 g/100 ml and a baby requires 1 g of protein per pound in 24 hours. Plasma should be used at half strength, making it up first in the ordinary way with distilled water and then diluting with 5 per cent glucose and 1/5 normal saline. By this means the solution will also approximately cover the maintenance saline needs.

Vitamin K.

1 mg of vitamin K should be given daily when the infant is being completely maintained on intravenous therapy.

ROUTE OF ADMINISTRATION

Intravenous.

Scalp vein intravenous transfusions are much more satisfactory than cutting down on a vein provided the anaesthetist does not object to their use. By the use of a plaster of Paris splint the needle can be held so rigidly that it is unlikely to come out of even the smallest vein. The fluid should be given as a drip unless the baby is very dehydrated, in which case up to 10 ml/lb. can be pumped in with a syringe in the first hour. If the baby is dehydrated it is unnecessary to wait for results before starting treatment. In these babies 5 per cent glucose and 1/5 normal saline should be given without delay.

The normal rate of fluids given intravenously should not be more than 5 ml/lb./hr and 3 ml is often adequate. If it is essential to cut down on the vein a Bateman's needle is more satisfactory than plastic tubing, since the latter sometimes pierces the vein wall some distance from where is has been inserted and if this happens a long length of vein has been rendered useless.

Subcutaneous route.

The writer finds that he has now largely given up this route because of the increasing skill in scalp vein technique of the resident staff. The subcutaneous route is unsatisfactory in that it causes the infant a considerable amount of discomfort and glucose should never be given because of the risk of necrosis and sloughing. The subcutaneous should therefore only be regarded as an alternative to the intravenous route if a scalp vein cannot be used and when it is not desired to expose a vein by cutting down.

Rectal route.

There is still a place for rectal fluids where, for example, an infant is vomiting but does not have diarrhoea. It is usual to give tap water in a dose of 30 to 90 ml every 4 to 6 hours.

Blood transfusion.

The amount of blood to be given should be calculated on the basis that a normal baby has 40 ml of blood per pound of body weight. If the

haemoglobin were 50 per cent then the baby would be deficient of 20 ml/lb. and the amount to be given can easily be calculated.

SPECIFIC CONDITIONS

Pyloric stenosis.

It should be possible to obtain perfect electrolyte control before operation since this is never an emergency procedure although it is often most urgent to correct dehydration and electrolyte imbalance. By a combination of the utmost attention to pre-operative therapy and the skill of the surgeons and anaesthetists, 172 consecutive babies have been operated on in this hospital in the last 8½ years without a death. Important in the pre-operative management of these babies is the stomach washout and should this produce a dirty result it is repeated up to three times a day before operation. In the postoperative period these babies are watched particularly carefully for the first 2 hours because of the danger of collapse, which has occurred in a number of babies during this period. These have been patients whose condition on admission was bad but whose electrolytes had been corrected before operation. On some occasions this postoperative collapse has been associated with an unusually deep level of anaesthesia and it seems that it may be related to retention of carbon dioxide in association with poor ventilation after the operation. The babies are cold and it is for this reason that there is always anxiety to ensure that they are kept sufficiently warm in the operating theatre.

Intestinal obstruction in the newborn.

Here again it is important not to hurry surgical treatment before the child is in correct electrolyte balance. Recently 2½ days was needed to ensure such correction before operating on an infant with duodenal atresia who then went on to make an excellent recovery.

Tracheo-oesophageal fistula.

This problem is somewhat different because of the risk of aspiration of saliva into the lungs, despite posture and suction. Although, therefore, there is less time available than in the baby with duodenal atresia it is felt that there is no need for an emergency operation at night and that it is better to delay treatment until the daytime.

Collapsed child.

The staff must be impressed with the need for aspiration of the pharynx in these children since so often the collapse is due to, or associated with, the inhalation of mucus. This point should also be emphasized to general practitioners, who should be able to aspirate mucus from the pharynx with an ordinary mucus catheter. On several occasions practitioners have most heroically rushed into hospital with a moribund baby with pneumonia but have not carried out this most urgent emergency measure. There is a place for intravenous hydrocortisone and oral cortisone in the treatment of collapsed babies and it should be remembered that cortisone given by mouth acts more rapidly than if given intramuscularly. Nikethamide is overrated; it is often given in a dangerously large dose which may cause convulsions, and before the child has been adequately cleared of secretions. If the air passages are not clear the deep inspiration produced by nikethamide causes a great deal of debris to be inhaled into the lungs.

It is necessary, in conclusion, to emphasize once again the need for respect for the child's delicate electrolyte balance.

ACKNOWLEDGMENT

I would like to thank Dr. John Black for his assistance in the preparation of this paper.

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A METHOD OF MEASURING ARTERIAL CARBON DIOXIDE TENSION DURING ANAESTHESIA

BY

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A GREAT number of operations are carried out under anaesthetic techniques using relaxants and controlled respiration. However, delay in the return of adequate spontaneous respiration occasionally occurs. Such a situation may be due to many factors (Paton, 1958), and the subject has been admirably reviewed by Churchill-Davidson and Wise (1960), who described a simple nerve stimulator by which the presence of residual nerve block may be demonstrated and the different types distinguished. As Churchill-Davidson and Wise (1960) point out, information about the arterial carbon dioxide level has been denied the clinical anaesthetist because of the technical difficulties involved, which are increased by the presence of anaesthetic gases and vapours, particularly nitrous oxide.

Campbell and Howell (1960) have described a simple method by which the arterial Pco_2 can be rapidly estimated with a high degree of accuracy, using the rebreathing technique. The analysis was carried out using a simplified Haldane apparatus (Campbell 1960). Twenty per cent potassium hydroxide was used to absorb the carbon dioxide from the sample; unfortunately, this substance has a high affinity for nitrous oxide, and therefore the presence of this gas will nullify any attempt to measure the Pco_2.

However, Nunn (1958) has shown that nitrous oxide is not appreciably absorbed by saturated sodium hydroxide. In his experiments an all-glass Haldane apparatus was used. It was decided to measure the absorption of some of the commoner anaesthetics gases and vapours in Campbell's apparatus using saturated NaOH as the absorbent, in order to evaluate the usefulness of the method of Campbell and Howell for estimating the carbon dioxide tension of arterial blood during anaesthesia.

METHOD

Pure oxygen, nitrous oxide, a mixture of oxygen and cyclopropane, halothane, diethyl ether and trichloroethylene vapours were each passed into the analyzer and their absorption measured. The gases and vapours were obtained from a standard anaesthetic machine fitted with rotameters, Boyle-type vaporizing bottles and a Fluotec vaporizer. The accuracy of the flowmeter (for cyclopropane) was not checked, nor were the concentrations of the vapours given by the Boyle bottles. In the latter, the plunger was placed just above the surface of the liquid, which initially was at room temperature. The samples were analyzed immediately to minimize any diffusion through the rubber bags used to collect them. The measuring chamber of the analyzer was filled and emptied twice before taking the final sample. Each aliquot was mixed with the reagent twelve times, and the results are the means of five separate determinations.

RESULTS

Only diethyl ether was appreciably absorbed; the other gases and vapours were absorbed to a negligible degree (table I).

TABLE I

Mixture	Percentage of sample absorbed	Difference in partial pressure due to absorption
100% oxygen	0.03	0.21 mm Hg
100% nitrous oxide	0.02	0.14 mm Hg
25% cyclopropane in O_2	0.03	0.21 mm Hg
4% halothane in O_2	0.00	—
Diethyl ether in O_2	0.3	2.10 mm Hg
Trichloroethylene in O_2	0.08	0.57 mm Hg

To show the amount of absorption in the modified Haldane apparatus of some common anaesthetic gases and vapours. Results are the means of 5 determinations.

DISCUSSION

Even the 0.3 per cent absorption of diethyl ether, representing a change in tension of 2.1 mm Hg at S.T.P., is hardly likely to obscure the significance of the measured carbon dioxide level in an apnoeic patient.

Nunn obtained an average of 0.02 per cent absorption of 100 per cent nitrous oxide in saturated NaOH which approximates closely to our figures. Campbell found that serial determinations on the same sample did not differ by 0.05 per cent and this was also our experience.

It was found with some vapours that the absorption was greatest in the first determination and progressively decreased, as for example trichloroethylene (table II). This phenomenon was presumably due to the acid rinse or to the absorbent becoming saturated with the gas or vapour. Sufficient measurements on each sample should be made to obtain three, or at least two, constant readings.

TABLE II

Mixture	Percentage of sample absorbed
Oxygen and trichloroethylene	0.35
	0.05
	0.00
	0.00
	0.00
	Mean = 0.08

To show the decreasing absorption of serial aliquots taken from one sample.

Concentrated NaOH is fairly viscous and insoluble substances tend to collect on its surface. Therefore, when the apparatus is not in use, the level of the absorbent fluid should be so adjusted that it lies in the expanded bulb containing the glass tubes, well below the reference line. If the level of the absorbent is left at this line for any length of time, cleaning may become necessary.

The collection of a sample of gases using the rebreathing technique takes less than 5 minutes. It was found that 10 minutes was adequate time to perform three determinations on one sample.

SUMMARY

A modification of the apparatus used in the method of Campbell and Howell (1960) for estimating arterial P_{CO_2} is described. It was found that the commonly used anaesthetic gases and vapours were absorbed only to a minor degree, thus allowing estimations of the arterial P_{CO_2} to be made in the presence of anaesthetic gases.

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ANALGESICS AND ANTAGONISTS

Sir,—The question of whether the simultaneous administration of a narcotic and narcotic antagonist prevents the respiratory depression of the narcotic without interfering with analgesia is an important one, since such mixtures are already commercially available. Hossli and Bergmann (1960) in their study "A combination of analgesic and antagonist in postoperative pain" have made a meritorious attempt to answer this question. They stated, "The authors conclude that the addition of levallorphan in the above proportion gives almost complete protection against the respiratory depressant effect of pethidine without diminishing the analgesic effect and without increasing the incidence of side effects". These conclusions do not seem justified from their data.

Respiratory depression. The authors measured respiratory rate and minute volume in two groups of anaesthetized patients before and after intravenous pethidine or an 80:1 pethidine-levallorphan mixture. They then derived alveolar ventilation. The data were presented in the form of a figure. I have taken their data from this figure and presented them in table I.

TABLE I

Adapted from data of Hossli and Bergmann (1960)

	Percentage of control values					
	12 minutes after injection			22 minutes after injection		
	Respiratory rate	Minute volume	Alveolar ventilation	Respiratory rate	Minute volume	Alveolar ventilation
Pethidine alone	50	55	65	55	60	80
Pethidine-levallorphan	65	75	85	65	75	90

Even if their failure to measure arterial or alveolar carbon dioxide tension, and the lack of a crossover study to control patient variability, could be overlooked these data certainly do not represent "almost complete protection against the respiratory depressant effect of pethidine".

Analgesic activity. The authors failed to find a difference in the analgesic effectiveness of pethidine alone compared with the pethidine-levallorphan mixture. They concluded that levallorphan did not interfere with the analgesia produced by pethidine. An alternative conclusion is that their method was too insensitive to detect the difference which may have existed. That the latter is more likely is indicated by their own data.

Since the authors did not include standard deviations or standard errors their data cannot be tested statistically. However, they state that when they compared the mean analgesia scores for pethidine alone with the scores for mixtures containing the same amount of pethidine, they found no statistically significant differences. This included a comparison of the mean 4-hour score for pethidine 50 mg alone of 14.8 and for the mixture of 16.4. It can be surmised then that a difference in mean score of 1.6 was not statistically significant.

Their data have been rearranged as shown in table II in order to compare the mean scores of the 50-mg and 100-mg doses. The difference between 50 mg and 100 mg of pethidine alone was 1.8 on the 3-hour score and 3.7 on the 4-hour score. If these differences were statistically significant (greater than 1.6) then the similar comparison of 50 mg and 100 mg of the mixture were not (both less than 1.6). This would indicate antagonism of analgesia at the 100-mg dose level by the levallorphan. If none of these differences, even the 3.7, is statistically significant, then their analgesic assay technique was too insensitive to distinguish a 100 per cent increase in the dose of pethidine (50 to 100 mg). In this case, it could hardly be concluded that no antagonism of analgesia occurred. There is good evidence that

TABLE II

Adapted from data of Hossli and Bergmann (1960)

Drug	Pethidine analgesia score 50 mg	100 mg	Difference
	3-hour score		
Pethidine alone	13.3	15.1	1.8
Pethidine-levallorphan	13.5	14.4	0.9
	4-hour score		
Pethidine alone	14.8	18.5	3.7
Pethidine-levallorphan	16.4	17.6	1.2

a narcotic antagonist can antagonize narcotic analgesia both in animals (Winter, Orahovats and Lehmann, 1957) and in man (Eddy, Lee and Harris, 1959).

Side effects. The authors' failure to find a difference in the incidence of side effects in their patients comes as no surprise. It has been noted by others (Beecher, 1958) as well as ourselves that it is difficult, if not impossible to obtain quantitative data on the side action liability of narcotics from patients who have received the drugs in the treatment of pain. In such subjects side actions of drugs are confounded with, or concealed by, the manifestations of the disease under treatment. The marked discrepancy between the side action liability of oxymorphone as reported from patients who received the drug for pain, compared with side actions reported from a controlled study in patients without pain, illustrates the point well (Keats and Telford, 1960).

Under some circumstances the simultaneous administration of narcotics and narcotic antagonists can result in a lesser degree of respiratory depression (Eckenhoff and Oech, 1960). However, it still remains to be demonstrated that this can be accomplished without antagonism of the other actions of the narcotics as well, including analgesia. The primary question remains unanswered by the data of Hossli and Bergmann.

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Sir,—Commenting on our paper "A combination of analgesic and antagonist in postoperative pain" (*Brit. J. Anaesth.*, 1960, **32**, 481), Dr. Keats states that our data do not seem to justify our conclusion that the addition of levallorphan gives almost complete protection against the respiratory depressant effect of pethidine without diminishing the analgesic effect.

With regard to respiratory depression, the detailed figures were published in an earlier paper (Hossli and Bergmann, 1959). The respiratory readings that Dr. Keats tried to obtain from our graph were actually as shown in the accompanying table.

These figures make it evident that there was significantly less respiratory depression with the mixture of pethidine-levallorphan in an 80:1 proportion than with pethidine alone. On the other hand, it cannot be denied that, even with the mixture, there was still some degree of respiratory depression; this was more pronounced as regards respiratory rate than as regards minute volume or alveolar ventilation. This is in agreement with the findings published, for example, by Foldes, Zeedick and Koukal (1957).

	Percent of control values					
	12 minutes			20 minutes		
	Respiratory rate	Minute volume	Alveolar ventilation	Respiratory rate	Minute volume	Alveolar ventilation
Pethidine alone	48	66	68	51	70	68
Pethidine-levallorphan	65	74	79	67	87	90

Bearing in mind the practical clinical uses of narcotics like pethidine, we should not be too much concerned as to whether or not there is still slight respiratory depression with the mixture pethidine-levallorphan; however, it is of primary importance that such depression should remain within acceptable limits, ensuring adequate respiration. In this context, an initial reduction of the minute volume and alveolar ventilation to 60 per cent of the initial figure 3 minutes after the injection of the mixture, followed by a return to 70 per cent at 6 minutes, 75 to 80 per cent at 12 minutes, and 90 per cent at 20 minutes with the mixture compares favourably with the findings with pethidine alone. With the latter, the comparable figures were: 30 per cent at 3 minutes; 43 per cent at 6 minutes; 70 per cent at 12 and 20 minutes. Such findings might certainly be interpreted as showing that the addition of the antagonist gives "almost complete protection" against the respiratory depressant effect of pethidine. I must, however, admit that a more cautious term such as "considerable protection" might have been more appropriate.

On analyzing our data concerning the analgesic activity by comparing the difference between pain relief scores for the 50-mg and the 100-mg doses of pethidine alone and the mixture, Dr. Keats suspects that antagonism of analgesia had occurred. Statistical analysis revealed that, whereas the difference in the score (3.7) between 50 mg and 100 mg pethidine alone at 4 hours is statistically significant, the 1.8 difference in the 3-hour score, although very near to the limit, is not. If we doubt the validity of Dr. Keat's arguments, this is not because of the lack of statistical significance of this latter figure. In fact, the validity of a comparison between the three dosage groups would depend on whether the various doses of 50 mg, 75 mg or 100 mg of pethidine had been administered to the patients in random order. This, however, was not the case in our study. In fact, the dose of pethidine was adjusted to each patient according to his body weight, general state and, in particular, the severity of pain. Therefore, under the conditions of our study, the comparison between pethidine alone and the mixture can only be made for each dose level separately, but not between different dose levels.

We are of course, aware of the fact that not only respiratory depression but also the analgesic and other effects of narcotics can be antagonized by narcotic antagonists provided that enough of the antagonist is given. The aim of our investigation, however was to find out whether interference with analgesia occurred when a particular narcotic-analgesic mixture was used in the proportions of 80:1. I do not deny the possibility that our method was not sensitive enough to detect minor differences which might exist between the analgesic activity of pethidine alone and the mixture. However, if such a difference actually existed, it was of a minor degree and had no clinical importance.

There is supporting evidence, or at least a strong suggestion, that the addition of levallorphan to pethidine in proportions between 100:1 and 50:1 does not interfere with the analgesic effect of the narcotic in the work of Schiffrin, Balagot and Sadove (1957) who, in a controlled study similar to ours, could not find any appreciable difference in the analgesic effect, in postoperative pain, of pethidine alone or mixed with levallorphan in the proportions of 100:1, 100:1.5 and 100:2.

G. Hossli
Zürich

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VOMITING AND HEAD-UP POSITION

Sir,—The interesting and instructive correspondence on this subject which has appeared in your Journal (Sykes, 1960; Hodges, Tunstall and Bennett, 1960) has not elicited an important criticism of what might be called the "posture and paralysis" technique for inducing anaesthesia in "emergencies". It has been suggested that the technique depends for its safety and effectiveness on speedy intubation and that if intubation proves impossible the patient is then in an extremely hazardous position. Now, although the conditions provided by suxamethonium paralysis usually render intubation simple, even for a relatively inexperienced anaesthetist, there are occasions when intubation may be impossible. An illustrative case was that of an old lady with very gross Paget's disease of the skull and face. Although this patient was able to open her mouth quite widely, it transpired, on attempting endotracheal intubation using the "posture and paralysis" technique, that the much thickened upper jaw so protruded over the small lower jaw that laryngoscopy was impossible, since only the uvula and posterior pharyngeal wall could be visualized, at best. This is a situation which might be dreaded at first thought but in fact nothing has been lost. A large-bore stomach tube must be passed into the stomach, which manoeuvre is simplicity itself if the tube is lubricated along its whole length. The stomach should then be aspirated to remove any fluid and now the patient must be turned on his side and tilted head down. The situation is at this stage almost precisely the same as if a head-down technique had been used from the start, except that the patient is still paralyzed and pulmonary ventilation through an airway and face-piece with an anaesthetic mixture is required until respiration is adequate.

If regurgitation occurs the situation is under control and the patient cannot endanger himself by laryngospasm or jaw clenching. If vomiting occurs when muscle power returns, the patient is no worse off than if it happened during an inhalation induction in this position and, since the level of anaesthesia is probably deeper than would have been the case during an inhalation induction, vomiting is much less likely.

Pre-oxygenation is obviously an essential part of the technique.

Thus it seems to me that the fear that intubation might prove impossible, which still deters some from using the "posture and paralysis" technique, is nothing more than a bogy which disappears when brought into the light of reason.

J. C. AINLEY-WALKER
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Sir,—I have read with interest the article on "Antihistamine drugs in pre-anaesthetic medication" by Erwin Lear et al. (*Brit. J. Anaesth.*, 1960, **32**, 582). They point out that as far as trimeprazine is concerned, 77 per cent of patients were adequately sedated but no analysis is presented of the remaining 23 per cent, who presumably were either apprehensive or disorientated. I feel it unfortunate that they did not use atropine only, or no premedication at all (placebo), for their control.

In a double blind trial using atropine only and trimeprazine with atropine in a series of 200 children prior to induction of anaesthesia for tonsillectomy, it was found that in children aged 6 years and over there was no significant difference in the percentage of calm, disturbed or turbulent children between those who had received trimeprazine orally in a dose of 2 mg/lb. body weight, 1½ hours pre-operatively and those who received atropine only, as shown in the accompanying table.

Premedication	% calm	% disturbed	% turbulent
Atropine only (1/100 grain)	44	31	25
Trimeprazine and atropine (1/100 grain)	45	28	27

It is my impression that, as yet, there is no satisfactory premedication short of basal narcosis for the inherently apprehensive type of patient.

W. N. ROLLASON
Aberdeen

INSTITUTE OF DENTAL SURGERY

Programme of a

CONFERENCE ON DENTAL ANAESTHESIA

June 8 and 9, 1961

1ST DAY

9.30 a.m. Address of Welcome—
Professor R. V. Bradlaw, C.B.E.

9.45 a.m. Symposium on Intravenous Anaesthesia
Chairman: Dr. Ronald Jarman, D.S.C.
Openers: 1. Dr. Douglas Young
2. Dr. M. Swerdlow

11.00 a.m. COFFEE

11.15 a.m. The Difficult Patient.
Chairman: Professor Ronald Woolmer
Openers: 1. Dr. W. S. McConnell
2. Dr. V. Goldman

LUNCH

2.00 p.m. Safety and Emergencies
Chairman: Dr. Patrick Shackleton
Opener: Dr. John Beard

3.15 p.m. TEA

3.30 p.m. Conditions in America
Chairman: Dr. F. W. Clement
Opener: Dr. K. C. McCarthy

RECEPTION AND DINNER AT ZOOLOGICAL GARDENS

2ND DAY

9.30 a.m. Legal Aspects of Dental Anaesthesia
Chairman: Miss K. G. Lloyd Williams, C.B.E.
Openers: 1. Sir William Bentley Purchase, C.B.E., M.C.
2. Surgeon Captain J. S. L. Coulter, D.S.C.

11.00 a.m. COFFEE

11.15 a.m. Dental Anaesthesia in the Services
Chairman: Dr. John Gillies, C.V.O.
Openers: 1. Surgeon Rear Admiral W. Holgate, O.B.E.
2. Major-General H. Quinlan, C.B.
3. Air Vice-Marshal, R. Scoggins, C.B.E.
4. Colonel K. Stephens, O.B.E.

LUNCH

2.00 p.m. Teaching of Dental Anaesthesia
Chairman: Professor R. V. Bradlaw, C.B.E.
Undergraduate Teaching:
1. Dr. T. Dinsdale
2. Dr. McGregor Rose

3.15 p.m. TEA

3.30 p.m. *Chairman*: Dr. Geoffrey Organe
Postgraduate teaching:
1. Dr. V. Goldman
2. Dr. Campbell Dewar

SATURDAY, JUNE 10

ADDITIONAL ITEM

10.00 a.m. and 3.00 p.m.
Edward Lumley Hall, Royal College of Surgeons: Closed Circuit Colour Television Demonstrations From Oral Surgery Department, Eastman Dental Hospital.

BOOK REVIEW

Illustrating Medicine and Surgery. By Margaret C. McLarty. Published by E. & S. Livingstone Ltd., Edinburgh. Pp. viii + 158. Price 37*s*. 6*d*. net.

In this book the author has done more than present an admirable treatise on the materials and methods of medical illustration; she has defined in a sentence (on page 92) the standard which all medical artists should achieve. She says: "All practising medical artists should be able to produce good operative drawings from a written or verbal description, from a drawing done by the surgeon, or from reasonable photographs."

With eye appeal becoming more and more part of our way of life it is natural that the teacher should wish to make greater use of visual presentation to reinforce his exposition of a subject, and that he should rely upon the artist's craft no less than on photography. This distinction Miss McLarty makes clear, showing how the camera can serve both the medical writer and the artist in no competitive way and how the artist can simplify or emphasize in accordance with the needs of the case.

Co-operation between two persons in any field can only be successful if each has some understanding of the other's problems, and from this book the competent artist will learn much of the specialized requirements of medical illustration. Similarly the medical author who needs to present a point visually be it in the form of a diagram, an informal sketch, or an elaborately detailed drawing, will benefit from reading an artist's presentation of her own side of the drawing board.

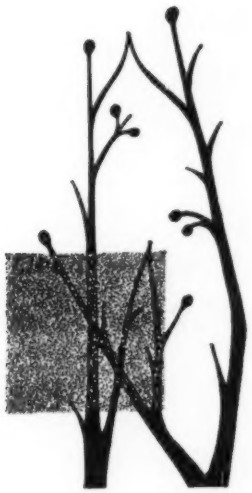
Much of the book is intended for those whose skill with the pencil is such as to make specialization in medical work a possibility. Types and techniques of drawing are examined and explained in detail, not omitting some of the more elementary but equally important matters of lettering and perspective, and at every stage illustration is made use of in exemplary fashion. The informative section on colour could with advantage lay more emphasis on the need for early liaison with the publisher and/or blockmaker, particularly as the limitations of the four-colour process call for restraint and understanding. As is mentioned in the section on "Some Probiems of Reproduction and Printing", the pigments used in printing inks are by no means perfect matches for the basic colours, and the artist's choice of a particular shade of crayon or paint may create reproduction difficulties which earlier advice from the engravers might have avoided.

From the point of view of the anaesthetist, neither he nor his subject, anaesthesia, appears prominently in this book. Nevertheless he will feel quite at home with it as there are no less than 23 pictures taken from the publications of Sir R. Macintosh and his collaborators, mostly from such well-known books as *Lumbar Puncture* and *Spinal Anaesthesia* and *Physics for the Anaesthetist*, volumes which most anaesthetists possess and with which all are familiar.

It will perhaps be useful for the sake of future editions of this excellent book to point out that the text references on page 132 to figures 166, 167, and 168, should be to figures 165, 166, and 167.

E. Falkner Hill

Printed in Great Britain by John Sherratt & Son, Park Road, Altrincham



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